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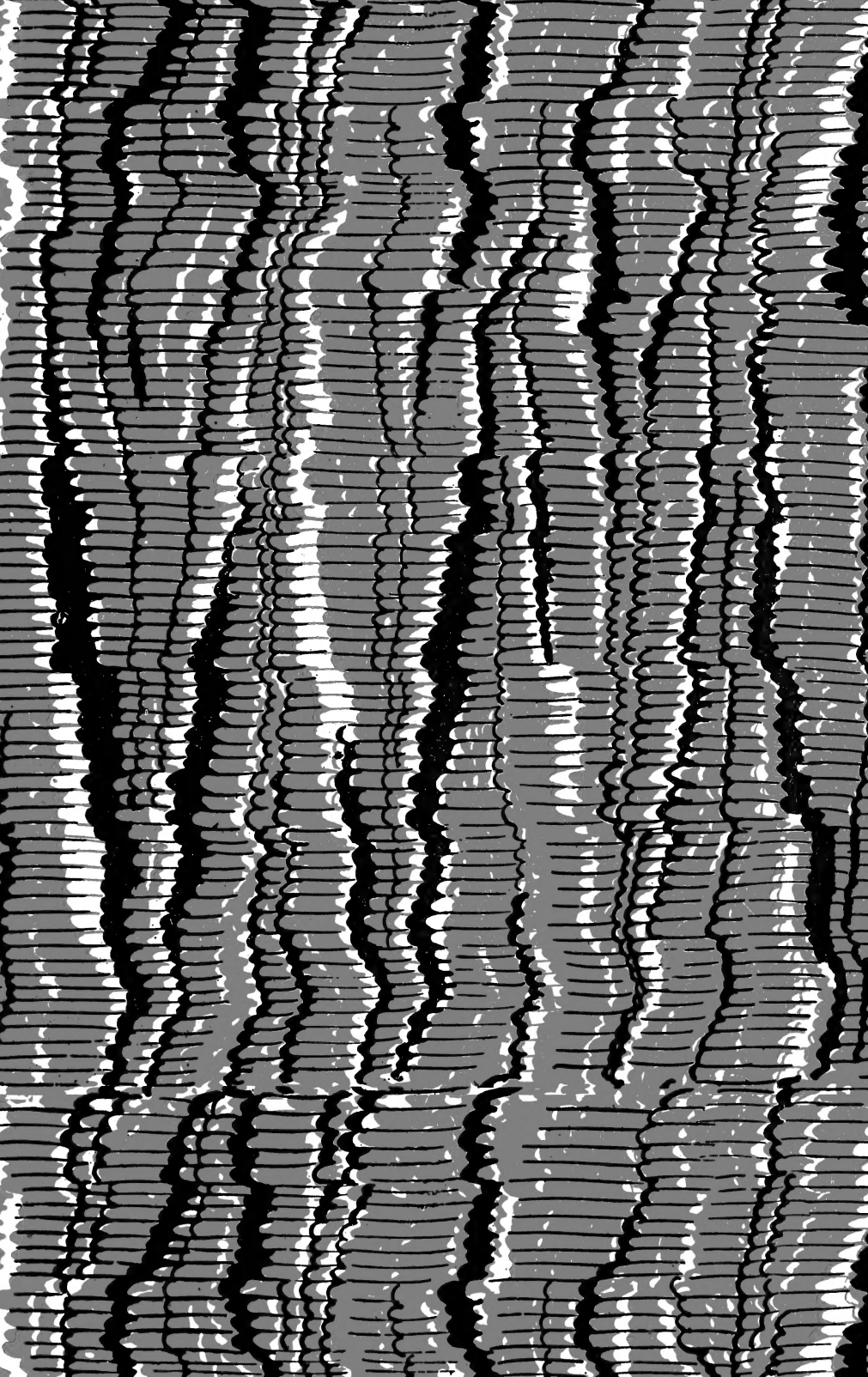
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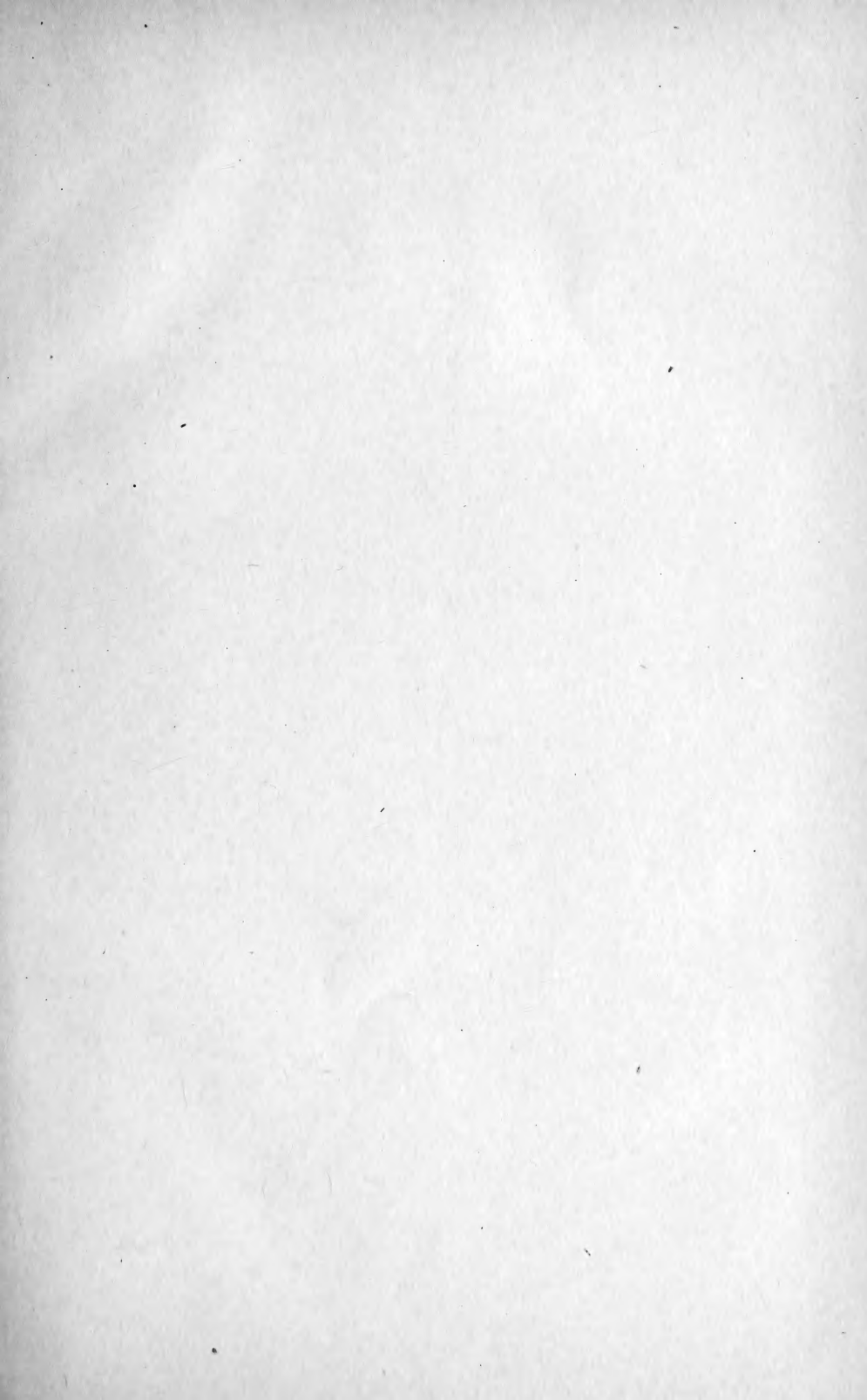




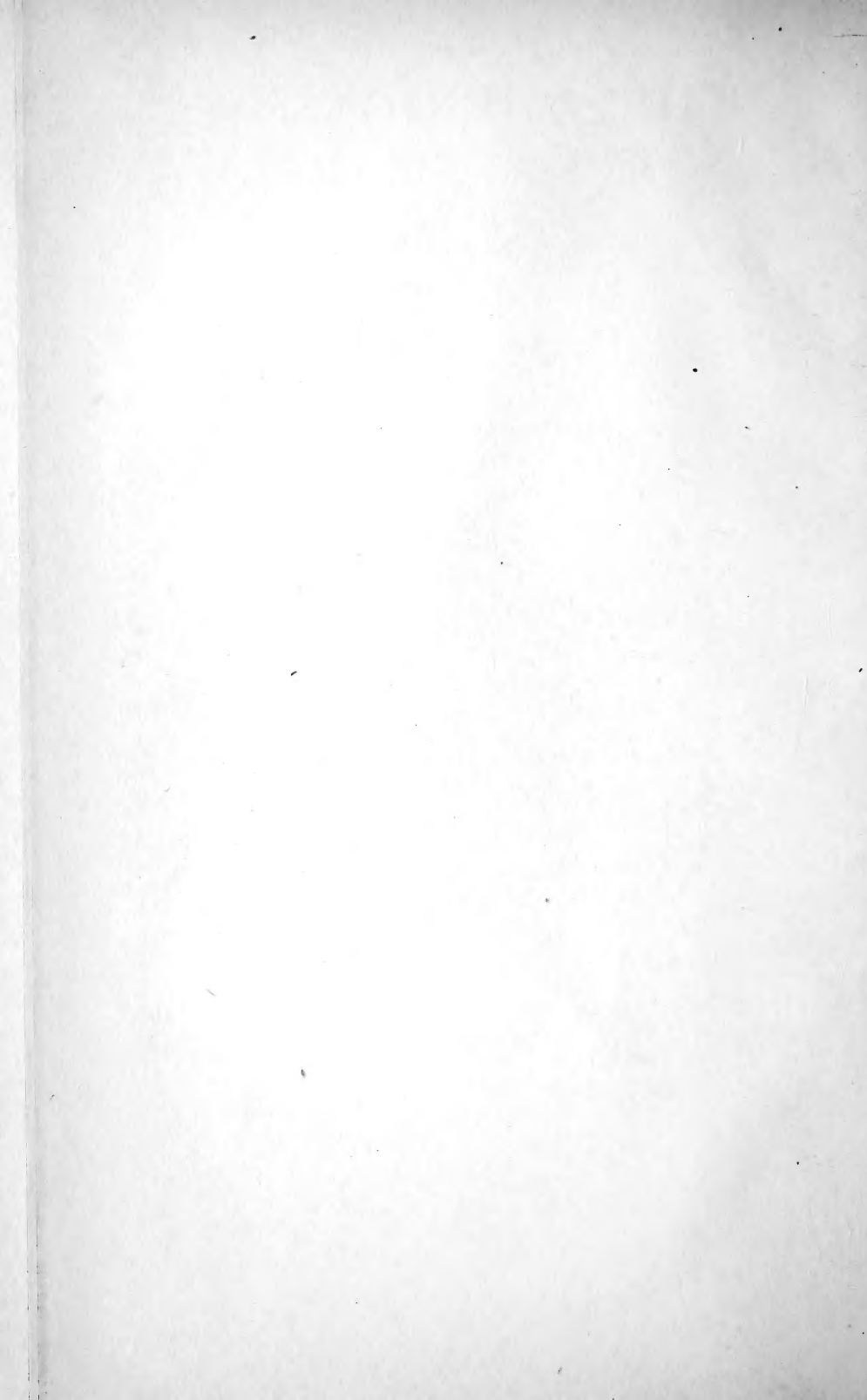












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# THE AMERICAN JOURNAL OF PHARMACY

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A RECORD OF THE PROGRESS OF PHARMACY  
AND THE ALLIED SCIENCES

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EDITOR

GEORGE M. BERINGER, A.M., Ph.M.

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# THE AMERICAN JOURNAL OF PHARMACY

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## EDITORIAL.

### ON THE THRESHOLD OF 1920.

"Time, as he passes us, has a Dove's wing,  
Unsoil'd and swift, and of a silken sound."

By the immutable laws of the Solar System another annual cycle has been completed and we are brought to the dawn of a new calendar, another Gregorian year. Before an appreciative, broad view of the expanse before us, a very brief retrospect of the year just closed may not be amiss. We are not prepared to-day to subscribe to the sentiment that

"What's past, and what's to come, is strewn with husks,  
The formless ruin of Oblivion."

The year 1919, despite the fact that it did not bring to fruition the anticipated reign of established Peace on Earth and universal Good Will among mankind, has not been lacking in actual accomplishments. Despite the fact that the demoralization of the most gigantic of all wars has been followed by a year of unprecedented social and economic disturbances and world unrest, there has been written in the historical chronicles of 1919 much that bespeaks real progress, much that is vital to the destinies of many nations and the welfare of millions of human beings. These events can never be obliterated from the records of the year nor buried in oblivion.

The wise statesmen and the thoughtful men of all civilized nations realize that the gigantic problems of this period of titanic reconstruction are necessarily being carried over to the new year and that the world's peace, prosperity and progress is dependent upon the wisdom and the justice of the decisions of these.

In matters pharmaceutic, the events of the year past have been encouraging. The conventions of the national pharmaceutical organizations of England and of America evidenced intense interest

in all of the various activities that make for the progress of the profession and the papers presented and the several addresses of the presidents and the chairmen of the sections indicated the earnestness of the spirit of research and the desire for professional advancement that pervaded these meetings.

Before closing the door upon 1919, we cannot refrain from referring to some matters that are personal to the JOURNAL. Volume 91 has been completed, but not without many peculiar and trying difficulties. Those who, during this year, have been engaged in publication or had dealings with printers will appreciate the troubles of the editor in endeavoring to have the monthly numbers of the JOURNAL issued with at least some degree of regularity. At times, it would appear as if the entire printing establishment was under the control of the "printer's devil" and that his main weapon was obstruction. However, the year with its trying, yet profitable, experiences is over.

The Editor has given his best efforts to maintain the AMERICAN JOURNAL OF PHARMACY as a progressive and ethical magazine of pharmacy and appreciates the support that has been given so loyally and continuously by the contributors and subscribers and is grateful for the encouragements and kindly expressions that have come his way. It is a great satisfaction to know that the JOURNAL is not only maintaining a long established ethical standard, but that, likewise, its advertising patronage and its subscription list are both making healthy and substantial gains, that its readers are multiplying and its influence is growing apace. He takes this opportunity to once more acknowledge his indebtedness to the authors and contributors who have aided so materially in the progress.

As we view the year ahead of us, we cannot but see the dark clouds that are already above the horizon. However, we are not inclined to be pessimistic. This year will be full of opportunity for work and for prosperity such as never came to us before. With optimistic energy we must seize the opportunities as presented, and with well-defined purposes work out the salvation of sane ideals that must be established as the foundation for social, economic and scientific progress. Pharmacists everywhere must realize that they will have a share in the responsibilities and opportunities of this momentous reconstructive period. The adherence to the ethics of the profession and the degree of personal application, will determine the individual's share in the prosperity and happiness that is in store.



The Pharmacopoeial Convention to be held in Washington in May, to prepare for the Tenth Decennial Revision of the United States Pharmacopoeia, will open to the medical, pharmaceutical and chemical professions many avenues for investigation and altruistic service. This should be the opening opportunity for marking the great progress in the medical professions during the decade that has passed since the previous Pharmacopoeial Convention convened. Every pharmacist should be in alignment with and participate in the work of the revisions of the Pharmacopoeia and National Formulary that will be commenced in 1920.

To our readers and friends we extend BEST WISHES and HEARTY GREETINGS and express the hope that the year 1920 will bring to them a bounteous measure of Prosperity and Happiness.

G. M. B.

#### THE BAYER COMPANY CITED TO APPEAR BEFORE THE FEDERAL TRADE COMMISSION.

In the August, 1919, issue of this JOURNAL, in an editorial on the "Proprieties of Advertising," reference was made to the objectionable style of newspaper advertising employed by The Bayer Company in advertising aspirin tablets and to the action taken by the Pennsylvania Pharmaceutical Association at its annual meeting in condemnation of same.

In this editorial, comment was likewise made upon the reply of The Bayer Company to the Pennsylvania Association, admitting error in the advertisement complained of and its discontinuance was announced. We directed attention to the fact that, although this admission of error was not as frank as might be wished, it was to be hoped that under the new management of this Company the questionable methods of advertising adopted by its Hun predecessor would be discontinued and that the modern standard of business ethics and the proprieties of advertising would be observed in the future.

We have since observed that this company has continued the extensive campaign of newspaper advertisements of aspirin tablets, and that many of these contain insinuations of the inferior quality of the products of other manufacturers.

The Federal Trade Commission has taken cognizance of this unfair method of advertising and formal complaint has been made alleging unfair methods of competition and The Bayer Company has

been cited to appear before the Commission and given forty days to file an answer, after which the case may be tried upon its merits. The Federal Trade Commission allege that the published advertisements of this company imply that the word "aspirin" is only properly used to designate the product of the respondent, and that its product is the only genuine, unadulterated and safe aspirin to be used, and that the products of other manufacturers, sold in competition as aspirin, are spurious and adulterated and composed of other materials, such as talcum powder and the like. By these actions it is alleged that The Bayer Company misleads the public into giving undue preference to Bayer aspirin, thereby causing loss and damage to competitors.

The action taken by the Federal Trade Commission raises an important question as to whether such advertisements are to be included in unfair trade methods and come within the control of this Commission. We await the outcome with the hope that it will firmly establish that proper methods are to be employed in advertising that will not be unfair to either competitors or to the public and indicative of a code of ethics worthy of fair-minded business men and maintain the properties of advertising.

There is still another question involved which may not be considered at all in the cause at issue. The question of the propriety of permiscuously advertising and encouraging the indiscriminate use of a drug which has at times a deleterious action upon the human organism. This important question must sooner or later receive consideration and possibly may have to be controlled by legislative enactments.

G. M. B.

### THE REVISED NARCOTIC REGULATIONS.

The Treasury Department, through the Internal Revenue, has issued Regulations No. 35 relating to the importation, manufacture, production, compounding, sale, dispensing and giving away of Opium or Coca Leaves their salts, derivatives, or preparations thereof. This pamphlet of 78 pages is a comprehensive exposition of the Act of December 17, 1914, commonly called the Harrison Act and the amendments thereof enacted as sections of the Revenue Act of 1918, and of the Regulations extant for the enforcement of these laws. It is a model "Regulation" for the thoroughness and clarity with which the Department has dealt with a difficult and intricate problem and presented its conclusions and instructions.

Commendable features of this public document are the classification of the subjects as set forth in the various headlines of the chapters and paragraphs and recapitulated in the "Table of Contents," the excellent index covering ten pages of titles and giving the numbers of the articles containing information relating to each item and the very general use of cross references in the articles themselves so that related information desired is readily and promptly obtainable.

These regulations are of the greatest importance to every one whose profession or trade activities necessitates the possession and handling of opium or coca leaves or any derivative or preparation made from or containing either. They are quite explicit and settle several mooted questions that had arisen under prior promulgations of regulations and contain some modifications of former rulings and a number of new features, the literal compliance with which may cause considerable annoyance and trouble.

The various articles of the regulations are titled and numbered and printed in juxtaposition with the provisions of the law to which they are intended to apply. We fear that some of these will be considered as entirely too stringent and as exemplifying the tendency of the Departments of the Federal Government to frame regulations that are bureaucratic exhibitions of authority rather than interpretations of the enactments of Congress for the *enforcement* of which regulations are authorized. It would seem at times that the police power was exercised by the officials in charge in ways that are unnecessarily burdensome and annoying to the many who are law-abiding and at no time would intentionally infract the laws, and that time, energy and official duty could be better applied in ferreting out and punishing the relatively few who are wilfully and criminally breaking the laws.

The purpose to have Federal and State enactments so dovetail as to prevent those who are not properly qualified from engaging in dealing in narcotic drugs is a fundamental principle to be observed. Very rightly an initial requirement is that only those whose dealings in narcotic drugs are not in violation of any law, either State or Federal, can be licensed under this law and that the application for registration must be accompanied by affidavit showing that the applicant is legally qualified or permitted, under the laws of the jurisdiction in which he is engaged, or proposes to engage, in any business or occupation within the scope of these regulations, to engage in such business or occupation.

Registrants under this Act should be careful to see that they carry on their business in these drugs in strict accordance with the classifications of the law and the differentiations of what can be actually done under each class. "A Retailer" cannot engage in the sale of original stamped packages of these drugs unless he likewise is registered as a wholesale dealer and pays the annual tax of \$12.00 imposed upon those so classified. Nor can a "Retailer" or a "Wholesale Dealer" engage in the manufacture and sale of non-exempted articles such as Laudanum and Dover's Powder without also registering under Class 1—Importers, Manufacturers, Producers, Compounders. As a consequence those engaged in a complex business, or who supply physicians and hospitals, for example, will have to be registered under several classifications and keep the required records for each. While a "Wholesale Dealer" under the definition of the Act may sell stamped full packages of other manufacture than his own, when he sells his own products of these narcotic drugs, he must do so as a licensed "Manufacturer" and stamp tax these at the specified rate of 1 cent for each ounce or fraction thereof of the *preparation* and not the narcotic contained.

Attention is especially called to the classification of chemists, who are not employees of a registered manufacturer, but who make analyses of narcotic drugs or preparations or use such in the analysis of other things, as liable to the tax as compounders of \$24.00 per year. They must procure the narcotic drugs to be used as test reagents in their analytical work on official order forms and keep records and make the same form of returns as do the manufacturers. This may be very unwelcome to the majority of chemists who but very seldom engage in such analyses or to the toxicologist who may unexpectedly be called into a case requiring such reagents to confirm his findings.

Practitioners who prescribe narcotic drugs must register and pay the tax of \$3.00 per annum even though they do not keep such drugs in their possession. A practitioner may sell to his *own bona-fide patients* narcotic drugs for legitimate medical purposes without incurring liability as a retailer.

Institutions, such as colleges of pharmacy, sanatoriums, clinics and hospitals not exempt as federal, state, county or municipal public institutions must pay the same tax as individuals similarly engaged in handling narcotics.

Itinerant vending or peddling is precluded as all sales and dis-

pensing must be done from a fixed address and a peddler of such drugs will be regarded as incurring a separate tax liability and committing an additional offense at each place where a sale is made. Even the exempted preparations may be sold only at or from registered places of business. This should eliminate the evil of the wagon peddler selling promiscuously paregoric and exempted proprietaries to the grocers and general store keepers who are irresponsible and usually not qualified by the laws of the state to engage in such trade.

Nurses are not permitted to register nor to be in possession of narcotics except as agents of physicians or those prescribed as medicines for their personal needs and they are subject to the same limitations as other consumers. A practitioner must account on his records for all narcotics left with nurses for administration and all such as are not administered must be returned to him.

While officials of national, state, county or municipal hospitals or public institutions, who in the discharge of official duties have to dispense or handle narcotics, are exempt from registration and the payment of the special tax imposed upon registrants, they must have the orders on which they secure the supplies of narcotics approved by the collector of the district and as a prerequisite satisfactory credentials of the exemption and official capacity of the official must be filed annually before July 1st. The exemption granted does not relieve them of the necessity of keeping the required narcotic records.

Ample provisions are made for change of address, change of ownership for any cause, and the mode of procedure in such cases is prescribed.

The forms for records and reports for each class of registrants are specified. The required records are exacting and the keeping thereof will entail much labor and may prove nigh impossible to the busy practitioner or dispenser. The reports are to be made out monthly and in triplicate, and exhibit all receipts of narcotics and their disposition and stock in hand.

Instructions are given for the cancellation and application of the special narcotic stamps to be applied by importers and manufacturers and the reports required provide for an accounting of all stamps purchased, used and unused.

The practicability as well as the wisdom of the requirement that narcotic drugs and preparations must at all times be segregated and be kept under lock and key, is questioned. While such a method may be readily practiced by a practitioner whose stock should be



relatively small and require but limited space, it will not be easy to follow by the druggists and manufacturers whose varied stocks and the ample supplies required would necessitate a large space, special compartments or rooms and each must be under lock and key. It will destroy the orderly classification and arrangement of stocks and moreover the segregation will advise the dope fiend and the thief where such valuable and narcotic drugs and medicines are stored.

Physicians and pharmacists want to bear in mind that official orders are to be issued for the purchase and transfer of narcotics and that duplicates must be made out at the time of executing the originals. Further, that they are to be used to cover each and every transfer of narcotics between those registered under the act, but they *must not in any case be used as prescriptions*. The order issued must specify the number and size of package of each item and if pills, tablets or other similar dosage forms, the number of such units in each individual package. The prior regulations are modified so as to permit a person licensed under several classifications to transfer on his records from one registry to another without the issuing of orders against himself, but his records must show every such transaction. Unfilled orders should be returned to the maker with a letter of explanation and this letter with the returned order is to be filed as part of his records. On orders filled in part only, the vender and likewise the vendee shall note on the order and duplicate the actual quantities supplied with date, and subsequent deliveries on account must also be noted on these orders.

Prescriptions can be issued for narcotics, only by practitioners duly registered under the act and can be filled only by pharmacists also registered under the proper classification. The regulations concerning prescriptions are necessarily exacting and must be carefully studied and followed by dispensers. A prescription can only be *issued for legitimate medical purposes*. *It cannot be issued as an order for the practitioner to purchase his supplies nor for the purpose of supplying addicts with narcotics*. *The prescription must be written with ink or indelible pencil or typewritten; if typewritten, it must be signed by the practitioner with ink or indelible pencil*. This may conflict with the custom in some dispensaries and clinics to have certain frequently-used prescriptions printed and with the not uncommon practice among physicians to use the ordinary lead pencil in writing prescriptions and not the indelible type now officially directed. *The prescription must be dated and signed the day of issuing*

*and must bear the full name and address of the patient, the name, address and registry number of the practitioner.* The responsibility for the proper writing of the prescription is upon the practitioner and he is liable to the penalties provided if he fails to insert thereon the information required by the law.

Physicians who have occasion to treat incurable diseases such as cancer and advanced tuberculosis where narcotics are necessarily prescribed in relatively large quantities, or who are attending aged and infirm addicts, the withdrawal of the drug from whom would result in death, are permitted to prescribe the narcotics needed in accordance with their judgment, provided endorsement is made upon the prescription that the drug is dispensed for the condition stated, and in the latter case give the age of the patient and state that the drug is necessary to sustain life.

The druggist filling the prescription must show on the back thereof the *signature and address of the person who secures the drug prescribed and must preserve the prescription for a period of two years.*

The *refilling* of a narcotic prescription is *prohibited*, except where the preparation covered by the prescription might have lawfully been sold in the first instance without a prescription or official order.

The permission to refill prescriptions for exempted drugs and preparations is a distinct modification of the previous regulations which differentiated between "prescription" and "preparation" and the selling of exempted drugs as either. *Partial filling of prescriptions will not be permitted under any circumstances, nor can prescriptions for narcotics be accepted over the telephone.* This provision will conflict with the custom of many physicians to telephone their prescriptions to the pharmacists.

The *order forms* supplied for the purchase and transfer of narcotics *must not be used as prescriptions.* The pharmacist filling the prescription must *affix to the package a label showing the name and registered number of the dealer, the serial number of the prescription and name and address of the patient and the name and address and registered number of the practitioner writing the prescription.* As containers frequently used for prescriptions will not be large enough to permit a label giving directions and also the additional data required by this regulation, it may be necessary to attach to the package a special label containing the data directed.

The collector of literary curios will find a number of these in the recent Congressional enactments and in regulations framed by the

departments. The following *bon mot* is a sample worthy of such preservation. "A practitioner is not regarded as in personal attendance upon a patient in the intent of the statute unless he is in personal attendance upon such patient away from his office."

"Personal attendance" should be irrespective of the temporary place of either physician or patient and the necessity of the patient should determine the drug prescribed by the physician and not the fact that the patient happens to be in the physician's office.

Only such narcotic drugs as are personally administered by a practitioner when in attendance upon a patient away from his office are exempted from the records of narcotic drugs required.

Stock solutions such as are used by oculists and other specialists may be kept on hand, providing a record is made of the date when the solution is made or purchased and the date when such solution is exhausted.

All records made by any of the registrants must be kept open for the inspection of authorized officials of the department.

The regulations provide that oral, nasal, ocular, rectal, urethral and vaginal preparations are not to be regarded as for external use, and that preparations manufactured or used for such purposes containing more than the exempted amount of narcotic drugs do not fall within the scope of the exemption granted to external preparations.

A private formula containing not more than the exempted percentage of narcotic drugs, made in accordance with a private formula of a physician, upon request of the physician that the druggist keep a quantity of the mixture on hand in order that prescriptions may be filled for his "special mixture" is not to be considered as a ready-made preparation in accordance with the U. S. P. or N. F. or established formula, and is, therefore not within the exemption granted for such preparations.

Every manufacturer, producer, compounder or vender (including the dispensing physician) of exempted preparations, must keep a record of all sales, exchanges, gifts, etc., the entries to be made at the time of delivery. The record must show the name, address and registry number of the dealer to whom the preparation or remedy is sold, exchanged or given, the name and quantity of the preparation or remedy, and the date on which the delivery to the purchaser or his agent is made. A separate record must also be kept of sales of such exempted preparations to persons other than dealers, even

though such sales are made on prescriptions. It is probable, that many druggists have not heretofore kept such record of the sales of exempted preparations and proprietaries, and they should take cognizance of the requirement of the law that such should be kept and the intent to enforce same as shown by the regulations.

G. M. B.

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## "PROOF SPIRIT"—WHAT IS IT?

BY RALPH R. FORAN, P.D.,

PHILADELPHIA, PA.

The term "proof spirit" is one of British origin, American adoption and universal confusion. In Allen's "Commercial Organic Analysis," 4th edition, we are told that "formerly the British Excise determined the strength of spirits by pouring a certain amount on gunpowder. A light was then applied. If the spirit was above a certain strength ('proof') the gunpowder ultimately inflamed, but if weaker the gunpowder was too much moistened by the water to be capable of explosion, and the sample was said to be 'under proof.' " Fortunately, this archaic method of approximating the alcoholic strength of spirits is no longer used, and by Act of Parliament, "proof spirit" is now defined to be a liquid of such density that, at 51° Fahrenheit, thirteen (13) volumes shall weigh the same as twelve (12) volumes of water at the same temperature. The "proof spirit" thus produced has a specific gravity of 0.91984 at 60/60° Fahrenheit, and contains, according to Fownes, 49.24 per cent. by weight or 57.06 per cent. by volume of alcohol.

The United States Internal Revenue Department defines "proof spirit" as "that alcoholic liquor which contains one-half its volume of alcohol of a specific gravity of seven thousand nine hundred and thirty-nine ten-thousandths (0.7939) at 60° Fahrenheit." "This will correspond to a specific gravity of about 0.9341 if water at 60° Fahrenheit be taken as unity and to a content of 42.7 per cent. by weight of absolute alcohol. Absolute alcohol would contain 200 per cent. of 'proof spirit' according to the United States system, instead of 175.25 per cent. in the English system."

This difference between the British and United States standards has served to bring about a pronounced confusion in the definition

of "proof spirit," and a survey of a number of text and reference books on pharmacy and the allied sciences has disclosed much misinformation on the subject.

Simon's "Manual of Chemistry," 11th edition, 1916, describes "proof spirit" of the United States Custom House and Internal Revenue Service as being identical with diluted alcohol U. S. P. Neither the diluted alcohol of the ninth revision nor that of any of the preceding revisions which were consulted is of "proof spirit" strength.

Wilcox's "Materia Medica and Therapeutics," 10th edition, and Culbreth's "Materia Medica and Pharmacology," 6th edition, 1917, also err in giving "proof spirit" as a synonym for Alcohol Dilutum U. S. P.

Remington's "Practice of Pharmacy," 6th edition, 1917, is authority for the statement that "United States proof spirit differs from diluted alcohol and is stronger; it contains 50 per cent. (or, more exactly, 49.5 per cent.) by weight of absolute alcohol." Surely this misstatement, in a book which is so widely read and quoted, will be corrected in the next edition.

Sadtler and Coblenz, in "Pharmaceutical and Medical Chemistry," 4th edition, 1918, have in mind the British standard and say that "proof spirit" has a specific gravity of 0.9198 at 15.5° C., and according to Fownes contains 49.24 per cent. by weight of alcohol."

In Leffmann and LaWall's "Organic Chemistry," 1904, "proof spirit" is defined as containing, by weight, "50.8 parts of absolute alcohol to 49.2 parts of water and has a specific gravity of 0.920." This would be correct for the British standard, were it not for the fact that the quantities of alcohol and water are transposed.

The most glaring misinformation on the subject is found in Gould's "Medical Dictionary." The 4th edition defines "proof spirit" as "any liquor containing at least 49 per cent. of absolute alcohol." In the 10th edition, 1917, matters are made worse by definition under two headings:

"Proof spirit—Alcohol containing 42.5 to 49.24 per cent. of absolute alcohol," and

"Spirit, proof—Dilute alcohol with 40 to 50 per cent. of pure alcohol."

Dorland, in his "American Pocket Medical Dictionary," 11th edition, 1919, uses these two definitions verbatim and is thereby guilty of perpetuating the fallacy.



Naturally, the majority of text and reference books have defined "proof spirit" properly. Where the subject has been elaborately treated, the suggestion is made that the term "proof spirit" be abandoned as being unscientific. This is a very proper and timely suggestion, and especially so, inasmuch as the coming era of prohibition will lessen the amount of spirits to be gauged. Whiskey, the liquid for which the gunpowder or "proof" test was originally devised, has fallen into disrepute and with it should go the term "proof spirit."

Finally, "proof spirit" is correctly defined as containing 50 per cent. by volume of absolute alcohol. This corresponds to 42.7 per cent. by weight. It has a specific gravity of 0.9341 at 60° Fahrenheit.

CHEMICAL LABORATORY,  
PHILADELPHIA COLLEGE OF PHARMACY,  
NOVEMBER 24, 1919.

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## NEW THERAPEUTIC USES FOR WELL-KNOWN CHEMICALS.

BY E. FULLERTON COOK, PH.M.,

PHILADELPHIA, PA.

*Benzyl Benzoate.*—In an extensive study of the action of opium alkaloids, David I. Macht, M.D., of the Medical Department of Johns Hopkins University, has demonstrated that these alkaloids divide into two classes, of which morphine is the most important of those belonging to the pyridin-phenanthrene group and papaverine, the principal representative of the benzyl-isoquinoline group.

The morphine group, including codeine, or methyl-morphine, dionine or ethyl-morphine, heroin or diacetyl-morphine, apomorphine, apocodeine, eucodine or methyl-codeine, peracodine or dihydrocodeine, and codeonal or codeine diethyl-barbiturate, all tend to stimulate the contractions and heighten the tonus of smooth muscles, but papaverine, or its related alkaloids, narcotine, narceine, and hydrastine, all produce an inhibition of the contractions of smooth muscles and lower their tonus.

He also fully proves that this action of the papaverine group was due to the benzyl portion of the molecule and this led to an effort

to find a non-narcotic benzyl combination which would produce similar therapeutic action and resulted in the discovery that the esters, benzyl acetate and benzyl benzoate, possessed such properties.

This was first shown by experiments upon animals and subsequently by many clinical tests and has led to the suggested use of the latter where antispasmodic action upon the smooth muscles is desired.

It was found that while the acetate was of equal therapeutic value it produced slight irritation upon the stomach and the benzoate has therefore been recommended for general trial. It is employed in dysentery, biliary, renal and uterine colic, in arterial spasms, bronchial spasms, as in asthma, in dysmenorrhoea and other excessive spasms of smooth muscles.

Benzyl benzoate has long been used as a solvent in perfumery, especially for synthetic musk, and also for the incorporation and fixing of the flavor in chewing gum, where it prevents loss by evaporation during the heating and kneading of the mass, and it is interesting to learn that its therapeutic value was suggested by chemical and physiological experiments, conducted in a modern research laboratory, whereby the value of such work is again conclusively demonstrated.

Pharmaceutically, benzyl benzoate must be treated very much like an oil. Its dose is small, 2 to 5 minims, and it has been most largely administered in 20 per cent. alcoholic solution containing 2 per cent. of soap which makes a solution that is readily miscible with water. It has also been dissolved in fixed oil and dispensed in capsules. Dr. Litzenberg (*J. A. M. A.*, 73: 601, 1919) suggests the following prescription for its administration for dysmenorrhoea.

R.

Benzyl Benzoate.....	10 mils
Mucilago Acaciae.....	5 mils
Elix. Eriodicty. Aromat. q. s.....	50 mils

Give from one-half to two teaspoonfuls as necessary. In the *J. A. M. A.*, 73: 599 and 601, a more extensive review and many additional references may be found.

*Benzyl Alcohol (Phenmethylo).*—During experimental work on benzyl combinations, in the study of their antispasmodic action,

Dr. David I. Macht (Pharmacologic Laboratory of Johns Hopkins University) incidentally tasted a minute quantity of benzyl alcohol and discovered that his tongue was completely anesthetized by it, the numbness, coolness and hardness, similar to the action of cocaine, continuing for over two hours.

This accidental discovery was followed by numerous experiments on animals and subsequently in minor operations and dentistry, with results that compare favorably with any of the known local anesthetics and in some respects greatly to the advantage of the benzyl alcohol.

Fortunately, benzyl alcohol is soluble in water and normal salt solution to the extent of 4 per cent. and this is sufficiently strong for use as a local anesthetic by injection. When used as an anesthetic in from 1 to 4 per cent. solutions in normal salt, it has never been found to cause any marked irritation or destruction of tissue, certainly less than that produced by equivalent amounts of cocaine or quinine and urea hydrochloride solutions.

The solutions may be sterilized by boiling without causing decomposition or loss of benzyl alcohol. When used on the eye it was found desirable to add a small amount of epinephrin (1 in 20,000), thus avoiding all irritation. A comprehensive study of its anesthetic and pharmacologic action will be found in the *Journal of Pharmacology and Experimental Therapeutics*, 1918, p. 263.

*Solution of Zinc Chloride.*—William Wayne Babcock, Lieutenant-Colonel in the Medical Corps of the United States Army, stationed at General Hospital No. 6, Fort McPherson, Georgia, has recently reported the successful use of solution of zinc chloride (prepared by saturating U. S. P. hydrochloric acid with zinc) in the treatment of chronic infected wounds of soft tissue and also of bone involvement.

The patients were all returned from the war areas and had already received months of treatment, usually with Dakin's Solution, and had been operated upon at least several times. The wounds showed a variety of infecting micro-organisms, and the solution of zinc chloride was used as a sterilizing agent, the tissue, which it simultaneously destroyed, being completely removed as a part of the operation. This procedure permitted the immediate closing of wounds, the avoiding of painful dressings, and a large percentage of permanent recoveries.

The technique is as follows, the operation being conducted under local or general anesthesia:

*Wound Preparation.*—The wound areas having previously been thoroughly cleansed by daily washing and shaving, the skin is thoroughly scrubbed with a solution consisting of 2 parts of compound solution of cresol, 10 parts of oil of turpentine and 88 parts of gasoline, and then painted with 3 per cent. tincture of iodine.

*Wound Sterilization.*—Immediately after the cleansing, the sinuses, cavities and wound surfaces are sterilized by the use of the solution of zinc chloride, injecting it under pressure, or packing with cotton pledgets dipped in the solution, and great care is taken to see that all unhealed and granulating surfaces are reached.

Five minutes is allowed for the penetration of the zinc solution, and if it has been injected, under pressure, into bone sinuses, a tourniquet must be applied and the solution allowed to enter the circulation only slowly, otherwise collapse will result. Because of the caustic character of this solution and the danger of direct introduction into the circulation it cannot be used in fistulas connected with the bladder, or intestine, nor can it be used in the presence of erysipelas, or other acute spreading infection.

*Color Dilineation.*—At the end of five minutes, the following solution is applied, in the same manner as the zinc chloride solution:

Saturated Alcoholic Solution of Methylene Blue.....	20
Potassium Hydroxide.....	3
Phenol.....	5
Ether, sufficient to make.....	100

When this solution evaporates it leaves the exposed granular surfaces dark blue-black, dry, bloodless on manipulation, and sterile, and beneath a grayish white tissue which has been sterilized and devitalized by the zinc chloride.

*Excision of Infected Area.*—The entire diseased area is now removed, the wound closed, and a moist, non-irritating, antiseptic dressing applied for the first week, or until all tissue reaction has subsided. The solution used consists of:

Hydrated Chloral.....	1
Alcohol.....	10
Glycerin.....	25
Saturated Solution of Boric Acid.....	65

This is injected into the gauze dressings every two or four hours by means of rubber tubes which are inserted when the dressing is applied.

The part where the operation occurred should be kept quiet, elevated and warm, and there should be no probing, squeezing, or introduction of tubes. The dressings should be changed daily and the adjacent skin must be kept clean and coated with a 2 per cent. yellow mercuric oxide ointment.

NOTE.—The details of this treatment and the formulas have been taken from a report on the subject read by Dr. Babcock at the recent meeting of the A. M. A. but not yet published.

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## DENATURING OF BAY RUM AND TOILET WATERS.

BY GEORGE M. BERINGER.

At the conference in Washington on December first, between the Prohibition Commissioner and members of the Technical Staff of the Bureau of Internal Revenue and the manufacturers of perfumery, toilet articles and barber supplies, it developed that the Department had made up its mind that bay rum and toilet waters made with non-beverage alcohol hereafter must be denatured by the addition of some modifying substance that would render these toilet articles unfit for beverage purposes.

Chief Chemist Adams, of the Bureau, stated that the Department was favorably considering a requirement that one-fourth grain of tartar emetic must be added to each fluid ounce of bay rum and toilet waters. The opinion of the Department as to the feasibility and safety of the use of tartar emetic as a denaturing substance was based upon a few days' trial in a way that could not be at all considered as worthy of the designation of a scientific investigation. No effort has been made to determine whether absorption followed the external application of bay rum so medicated or whether there was any evidence of the poison having entered the system or of its elimination through the secretions.

The technical experts present were unanimous in their objections to the use of tartar emetic and pointed out its toxic action and the danger of poisoning either through accidental or intentional consumption as a beverage.

It is to be regretted that in the face of this information and with

only such a scant investigation the Department should persist in further advocating the addition of tartar emetic in this quantity as a modifying agent for this class of toilet preparations.

We note a published statement that the Department has decided that "No application to use non-beverage alcohol in the manufacture of bay rum without regard to alcoholic content, or of toilet waters containing less than 50 per cent. of alcohol, will be approved by the Internal Revenue Bureau, after January 16, 1920, unless same are modified by the addition either of one-fourth grain of tartar emetic to the fluid ounce or a satisfactory quantity of some other modifying agent to be suggested by the manufacturer, who in presenting the suggestion to the Bureau, shall submit sufficient data to satisfy the officials of its efficiency. The requirement placing the burden upon the manufacturer to make the necessary tests of the modifying agents proposed as alternatives is made necessary because of the small technical staff at the disposal of the Bureau."

For more than three hundred and fifty years antimony has been recognized as a poisonous metal, and all its salts as active poisons. Its close relation chemically to arsenic and the analogy between the symptoms produced by arsenic and antimony have long been recognized. It is not safe to rely upon the probability of emesis to eliminate tartar emetic, as it is a well-known fact that at times there may be a complete absence of vomiting or only a slight nausea, but the toxic action of the drug may later be exhibited in other ways than by vomiting and diarrhea. Paralysis as well as direct action on the heart and respiration and convulsions are among the symptoms that have been recognized, even from moderately small doses, and as little as one-third of a grain is recorded as having caused death. Even when applied externally it has been known to produce local irritation and pustular eruptions.

It is not improbable that the continuous external application of a toilet water so medicated may produce chronic antimonial poisoning, nor is it at all certain that such use would not have a deleterious action upon the hair as well as the skin.

It is inexplicable that, in the light of recent experience and the numerous deaths resulting from the use of poisoned whiskey substitutes, a department of the government should propose the use of such a toxic agent for the denaturing of toilet waters for the purpose of preventing their possible consumption for alcoholic beverages.

At the conference of the technical experts present in Washington a number of materials were discussed as possible modifying agents for this class of preparations. Among those mentioned were the chlorides of zinc and cadmium. Objections were made to the use of these mineral salts upon the ground that they would possibly act upon and modify the perfume constituents, and also cause precipitates in the preparations, and there was likewise an uncertainty as to the toxicity of these salts.

Saccharin in relatively large quantities was suggested as a modifying agent. The extreme, disagreeable sweetness and acidity that this would produce would possibly render such medicated bay rum or toilet water unfit for beverage purposes, but the persistent sweetness produced when applied to the face and lips would be objectionable and render the product unfit for its legitimate use.

Formaldehyde was another of the possible agents considered, but objection was made as to the possibility of this having a deleterious action upon the perfume oils and chemicals of the formulas.

Salicylic acid was another suggestion that did not meet with a cordial reception because of its proneness to react with other chemicals and to undergo change and possible darkening in solution.

Phenolphthalein was suggested by someone, but its well-known color reactions with alkalis preclude serious consideration. After shaving or washing with soap the application of a toilet water so medicated would produce a distinct purple or red discoloration of the skin as well as staining towels and clothing to which it might be applied.

Among vegetable drugs possibly useful as denaturants, soap bark and colocynth are worthy of consideration; the latter especially appears to give satisfactory results from our experiments. In the proportion of two grains to the fluid ounce it renders the filtered bay rum sufficiently disagreeable and unpleasant to render it unfit for beverage purposes and does not appear to affect injuriously either the color or odor of the preparation. It would appear as likely to serve as a suitable modifying or denaturing agent for perfumes and alcoholic liquid toilet preparations.

## A REVIEW OF THE ADVANCES IN PHARMACY.

BY JOHN K. THUM, PH.M.,

THE LANKENAU HOSPITAL, PHILADELPHIA.

THE ACTIVITY OF AMERICAN DIGITALIS.—J. H. Pratt and H. Morrison, of Boston, both doctors, had their attention called to the possibility of using American digitalis as early as 1910, when a tincture made from leaf grown in the Rocky Mountains was found, in their laboratory, to be nearly twice as strong as the tincture in use at that time in the Massachusetts General Hospital. This tincture was prepared by a prominent American manufacturing pharmaceutical house in January, 1909; and as it was not tested until December, 1910, it was probably two years old and had probably lost some of its original potency.

The authors mention that Duffield, in the *AMERICAN JOURNAL OF PHARMACY*, 41: 55, 1869, speaks of tests that he had made of American-grown digitalis, prepared by the Shakers of Mount Lebanon. By crude chemical methods he found that the percentages of active principles were higher than in samples of English leaf, and these in turn higher than in German leaves that he examined at the same time. He said that our home-grown digitalis, if properly dried and gathered, was superior. Unfortunately, his investigation led no one to study and report the therapeutic value of the American digitalis leaf.

In 1911, Dr. Hale published the result of some of his work which shows that first-year leaves from American leaves from Arlington, Va., and those grown in Madison, Wis., and Seattle, Wash., were stronger than the select English leaves that he tested at the same time for comparison. He also found that second-year leaves grown in Seattle were somewhat weaker than the English digitalis.

Rowntree and Macht (*Jour. A. M. A.*, 66: 870, 1916), using the cat method of Hatcher and Brody, made the discovery that digitalis from the drug garden of the University of Wisconsin was more active than any of four lots of Allen's English leaves tested. Some of this same lot of Wisconsin leaf was tested by Dr. Pratt, a 10 per cent. infusion being used. The Minimum Lethal Dose of this infusion was 0.012 Mil. per gram frog weight. Dr. Pratt states that this was stronger than the majority of English and German leaves examined in his laboratory. Roth tested some American-grown



digitalis and obtained results that compare favorably with that of any grown anywhere else. He believes that the wild digitalis which is found in the Northwestern States may be utilized as a source of supply for making the various preparations of digitalis and that by using ordinary methods in handling and preparing the leaves a highly active product may be secured, one that would compare favorably with the activity of cultivated leaves grown under more favorable conditions.

In their experimental work Drs. Pratt and Morrison used the one-hour frog method recommended by the United States Pharmacopœia. In one series twenty-two frogs were required to determine with sufficient accuracy the minimal dose required to produce systolic standstill. The temperature of the water in which the frogs were kept before and during the experiment was carefully regulated, and the temperature of the air in the room was noted and recorded. Twenty-eight samples of American-grown digitalis were tested. It is believed that differences in strength in leaves grown in different localities is due to soil and climate. Digitalis does not grow well on limestone lands. This was noticed by Lloyd when he tried to cultivate the leaf in Kentucky. It is generally found in profusion on land containing iron and manganese. Digitalis does not grow in Switzerland and it is attributed to lack of iron and manganese in the soil. The authors conclude that the best American digitalis, both wild and cultivated, is equal in activity to the best European digitalis. They are also strongly of the opinion that all digitalis should be tested biologically before it is gathered in large quantities for medicinal use.—*Jour. A. M. A.*, 73: 1606, 1919.

A CLINICAL STUDY ON THE USE OF CALOMEL INUNCTIONS.—Mercury inunction has been used for the treatment of syphilis ever since the beginning of recorded medical history, and always in the form of an ointment made with the metallic mercury. There has always been objections to its use, however, by fastidious persons, and justly so, on account of its uncleanness, its betrayal of what the patient is suffering from, and the frequency with which it sets up irritation of the skin. These points have been often dilated upon. Recently, Wile and Elliott and Schamberg, Kolmer, Raiziss and Gavron have suggested the use of calomel. Their reason for advocating its use is that it overcomes the foregoing objectionable features of blue ointment. As calomel is more cleanly, and as they

felt that it is as easily absorbed through the skin as the ordinary blue ointment, they advised that it be used for inunction purposes and advanced a formula consisting of:

Hydrargyri chloridi mitis.....	3.00 Gm.
Lanolini.....	1.00 Gm.
Adipis benzoinati.....	2.00 Gm.

The arguments of the above authors as to its absorbability seemed so convincing that Cole and Littman, of Cleveland, began to use it in their private practice. This was in the spring of 1917. Since then the use of calomel has become so popular that a manufacturing house has brought out an ointment of calomel which is a little more pleasant than the ordinary preparation, though probably no more efficient. After using this for some time Cole and Littman began to feel that it was not doing what was expected of it. For one thing, the patients never became salivated with it, which struck them as significant. They also noticed that many times patients did not react to this treatment as they had to blue ointment inunctions or injections of mercury. These results, or lack of results, led them to carry out a series of tests in a scientific manner to determine the efficacy of calomel inunctions. Fresh clinical syphilis in the venereal wards of the Cleveland City Hospital was used for the demonstrations. Tests on fifty-four cases were carried out in as unprejudiced manner as possible. The investigation was undertaken at the suggestion of the Therapeutic Research Committee of the Council on Pharmacy and Chemistry of the American Medical Association.

The cases were carefully watched: routine Wassermann tests on the blood, *Spirochæta pallida* examinations and spinal fluid examinations were made in every case. Care was taken in all instances in using the ointments that patients were always under the observation of an orderly or of a nurse to see that the inunction was rubbed in through a space of at least thirty minutes for six nights in each week, with a hot bath on the seventh night, and without other medication. In nearly all the cases the calomel ointment described above was used, it having been prepared by the hospital pharmacist. In a few cases a proprietary calomel ointment was used. It was often difficult to keep the patients under this treatment as long as the investigators would desire as some of them noticed that they did not improve under this manner of treatment. To quiet them they were given saline injection as a placebo so that they would be under

the impression that they were receiving arsphenamin medication in conjunction with the inunctions.

An analysis of the results show that there was practically never any improvement in primary lesions when these inunctions were used. The lack of salivation was in startling contrast to results after the use of the old reliable blue ointment. They conclude that calomel inunctions are almost completely inefficient against primary and secondary syphilis. Furthermore, such inunctions very rarely produce salivation or gingivitis. This means poor absorption and explains its clinical inefficiency. The calomel also produces dermatitis. The investigators strongly urge the discontinuance of the use of calomel ointment for the treatment of syphilis.—*Jour. A. M. A.*, p. 1408, 1919.

A NEW GERMICIDE FOR USE IN THE GENITO-URINARY TRACT: "MERCUROCHROME, 220."—Drs. Young, White and Swartz, of the Brady Urological Institute of Baltimore, have been making a study of antiseptics with the end in view of discovering something particularly applicable to the genito-urinary tract. Noting the results of the use of the flavines in the treatment of venereal diseases they became impressed with the possibilities of using dyes as a basis for the development of germicidal and therapeutic compounds, their object being to obtain drugs that would possess the penetrating qualities of dyes and at the same time be destructive to germs and comparatively non-toxic and non-irritating. This research resulted in a number of compounds and from among them the substance mentioned above was selected for extensive study. In "Mercurochrome, 220," the investigators assert they have evolved a drug of demonstrated germicidal value. The rapidity with which some old infections of the bladder, kidney and pelvis have been cleared up after its use is striking, and they lay special stress on its absence of irritating and toxic qualities, and the ease with which the patient may retain a one per cent. solution for hours without discomfort. This, they say, is more than sufficient to establish the possibilities of the drug in these conditions. They state this is the first time that a drug has been developed having great germicidal strength and which can be borne or tolerated in the human bladder for several hours. This is an ideal which has long been striven after. In synthesizing this drug they had in mind the production of one that would have the following properties: (1) Ready penetration of the

tissues in which the infection exists; (2) lack of irritation of the drug to tissues; (3) high germicidal activity; (4) ready solubility in water and stability of the solution; (5) freedom from precipitation in urine; (6) sufficiently low toxicity to avoid systematic effects from the small amount of the drug that may be absorbed.

Mercurochrome is obtained by substituting one atom of mercury in the molecule of dibromfluorescein. Chemically it is dibromoxymercuryfluorescein, or its sodium salt. It contains about 26 per cent. of mercury. The free acid is a red powder insoluble in water but readily soluble in sodium hydroxid solution, with the formation of a deep cherry-red color. Its solutions show fluorescence on dilution. The dry salt forms iridescent green scales, slightly hygroscopic and readily soluble in water. The solution is stable and is not affected by moderate heat or exposure to the air. Strongly acid urine gives a slight precipitate of the free dye. There is entire freedom from precipitation when a one per cent. solution of the drug is mixed with an equal volume of medium rich in protein such as hydrocele fluid. The solution stains the skin a bright red color, but this can be removed by rubbing first with a 2 per cent. solution of potassium permanganate, and then with a 2 per cent. solution of oxalic acid. In actual practice it has been found that this tendency to stain is annoying to patients in that extraordinary care must be taken in regard to underclothing, sheets and towelings, as it is impossible to remove the stains. A 1 : 1000 solution of the drug will kill *B. coli* and *Staphylococcus aureus* in urine in one minute. It has practically 50 times the germicidal strength of acriflavine in urine medium for exposures of one hour. Solutions of one per cent. can be held in the human bladder for from one to three hours without irritation. The drug has proved to be of great value in the treatment of chancroids and as a dressing after incision of buboes. It promises to be of great value in the treatment of gonorrhea. Its use in chronic affections of the bladder gave remarkable results, purulent cystitis disappearing in a surprising manner with freedom of pus and bacteria in a few days.—*Jour. A. M. A.*, Vol. 73, No. 20, 1919.

FIXED OIL OF FENUGREEK.—Besides an essential oil, fenugreek seeds contain about 7 per cent. of a fatty oil, color golden, and with a characteristic unpleasant smell and taste. Its specific gravity is 0.9471 at 15°C., saponification value 189.5, and iodine value 132.8.

According to the investigator this oil contains 6.25 per cent. of lecithin and 0.5 per cent. of phytosterins. The fatty acids are mainly linoleic and oleic acids, and 1.5 per cent. of volatile fatty acids. It was noticed that when the oil is spread in a thin layer and exposed to the air, it quickly dries to a golden yellow, transparent varnish, which is insoluble in ether. Therefore, it rightfully belongs to the class of drying oils.—H. E. Wunchendorff, *J. pharm. chim.*, 1919; through *The Pharm. Jour. and Pharmacist*, Aug. 16, 1919.

**BENZOIC ACID FROM COWS' URINE.**—No doubt due to the unsettled and chaotic conditions brought about by the Great War, an old source of benzoic acid has recently again been made use of. Since the discovery of the possibility of making this acid synthetically from toluol, the natural source does not appear to have been very much encouraged and rightly so as cost of production is a very important factor in manufacturing. However, it has been suggested by the authors of this paper that its manufacture is still commercially feasible in Canada. They found that hippuric acid equivalent to one pound of benzoic acid per diem is obtainable from fifteen cows. The urine is acidified with hydrochloric acid and cooled to 0° C., when the hippuric acid crystallizes out. They believe this process could be profitably worked out in winter by Canadian dairy farmers.—P. J. Moloney and F. T. Shutt, *Trans. Roy. Soc., Canada*, 1918–1919, 31, 12 (3), 149; through *The Pharm. Jour. and Pharmacist*, Aug. 16, 1919.

**MODIFIED FORMULA FOR CALOMEL PROPHYLACTIC OINTMENT.**—The claim is made by Duret that the following combination gives a preparation of far greater prophylactic value against syphilitic exposure than the original formula of Metchnikoff, which is now officially recognized in France. Duret's formula is as follows:

Precipitated Calomel.....	10.0
Crystalline Magnesium Chloride.....	10.0
Sodium Bicarbonate.....	7.0
Thymol.....	0.15
Camphor.....	0.35
Glycerole Starch.....	15.0
Nut Oil.....	15.0
Anhydrous Wool-fat.....	20.0
Distilled Water.....	25.0

This combination is brought together as follows: The magnesium chloride and sodium bicarbonate are triturated with the water; the calomel is added and then the glycerole of starch. The anhydrous wool-fat is melted with 10 grams of the oil; the camphor and thymol are now dissolved in 5 grams of the oil and added to the melted mixture; this then added to the calomel mixture and the whole thoroughly mixed in a mortar until a uniform mixture is produced.—P. Duret, *Annales Institut Pasteur*, 1919; *Répertoire de Pharm.*, 30: 196.

VENOM OF BEE STINGS.—M. Arthus noted that the symptoms produced by poisoning with the secretion from the poison glands of bees show that the venom is a proteotoxin. In many respects it is similar to scorpion venom. It has a hypotensive action, similar to the scorpion venom, and which is sometimes very considerable although it differs from this venom in that it has no sialagogue or mydriatic action. The investigator also noted rabbits treated with this toxin gave unmistakable evidence of having marked intestinal peristalsis.—*J. pharm. chim.*, 20: 41, 1919.

CONSTITUENTS OF LEMON JUICE.—R. Huerre, in an investigation of the juice of this fruit from three different lots of lemons, found that neither oxalic nor tartaric acids were present in the juice. The specific gravity ranged from 1.048 to 1.064. Expressed in terms of citric acid the total acidity was from 7.14 to 7.8 per cent. One hundred Mils. gave a yield of from 7 to 7.5 grams of citric acid; from 0.40 to 0.60 gram of malic acid; from 0.40 to 0.50 gram of cane sugar; from 1.8 to 2 grams of invert sugar; and from 1.6 to 1.8 grams of ash on incinerating the dry extractive.—*J. pharm. chim.*, 20: 1, 1919; through *The Pharm. Jour. and Pharmacist*, Aug. 16, 1919.

OIL AS A SUBSTITUTE FOR ALCOHOL FOR FLAVORING EXTRACTS.—An interesting suggestion is made by A. Thurston in the *Midland Druggist* in reference to the suitability of using fixed or fatty oils as solvents for culinary flavors in place of the heavily taxed and expensive alcohol. The approach of absolute prohibition makes some investigation along this line rather timely. He states that such oils as cottonseed, olive, or neutral lard oils will be found satisfactory for this purpose. In his estimation these fixed oils hold the flavor much better than alcohol. Their use also has the added advantage

that they act as shortening to any baked pastry. To make an oily extract of vanilla or tonka beans he advises that 1 part of the solid be heated on a water bath to from 70° to 80° C. with 10 parts of oil for 30 minutes, and then strained. If vanillin or coumarin is used he suggests that a solution of these can very readily be made in the proportions of 1 in 40 or 1 in 50; these will give a flavor about 10 times stronger than an oily extract of the beans.—*Midland Druggist*, 1919, pp. 53, 88.

INCOMPATIBILITIES OF STRYCHNINE SULPHATE.—Among the requirements of strychnine sulphate in the French Codex is one that it must be neutral, in contradistinction to the U. S. P. requirement which allows some latitude, it stating that strychnine sulphate should be neutral or slightly acid. A perfectly neutral salt naturally will be somewhat incompatible in a solution such as the following which is in great vogue among French physicians as a hypodermic injection: Sodium cacodylate, 0.50; strychnine sulphate, 0.02; distilled water, to make 10 Mils. At first this solution makes up clear but after a short time a crystalline precipitate of strychnine cacodylate slowly makes its appearance and adheres to the sides of the bottle or ampul. This is due to the lack of solubility in water of the strychnine cacodylate formed by double decomposition. There are a number of proprietary ampuls of this combination on the market which, although they have the correct amount of these very active ingredients, do not show any evidence of precipitation of this potent salt. This is brought about by substituting for part of the distilled water a small amount each of glycerin and alcohol. The modified formula for this injection gives a solution which is permanent and without any possibility of dangerous consequences.

Strychnine Sulphate.....	0.02
Sodium Cacodylate.....	0.50
Alcohol, 90 per cent.....	4.00
Glycerine.....	2.00
Distilled Water, boiled.....to make	10.00 Mils.

One Mil., which is the dose of this hypodermic injection, contains 5 centigrams of sodium cacodylate and 2 milligrams of neutral strychnine sulphate.—E. Cabannes, *Répertoire de Pharm.*, 30: 193, 1919; through *The Pharm. Jour. and Pharmacist*, Aug. 23, 1919.

BOTULISM: I.<sup>1</sup>

The striking symptoms and high fatality of botulism have given to this disease, as to rabies, an interest and a conspicuousness far beyond its relative importance as a cause of death. Two recent fatal outbreaks of "food poisoning," one in Ohio, the other in Michigan, have been attributed, it seems with justice, to botulism intoxication from ripe olives packed in California, and these tragedies have increased the uneasiness felt by some persons about the dangers from this cause. American investigators in the past few years<sup>2</sup> have added much to our knowledge of botulism, and several recent articles, especially, have helped to define the conditions under which this serious form of food poisoning may take place.

It has been shown that the name of botulism, or sausage poisoning, is quite inappropriate to this form of bacterial intoxication as it occurs in the United States. Canned string beans, asparagus, corn, apricots, ripe olives and cheese have been implicated at various times and places, while meat products have seldom been casually connected with such cases. Apparently, the majority of outbreaks on record in this country have been due to household canned foods, and one of the points in dispute has been whether a similar danger is to be feared from factory canned foods. The difference of opinion among workers in this field is exemplified by correspondence recently appearing in the JOURNAL from two correspondents.<sup>3</sup> Some of the points raised in the correspondence are of general interest.

There is no doubt that the early statements of van Ermengem, the discoverer of *B. botulinus*, about the low heat resistance of this organism are incorrect if applied to all conditions or all strains. Most of the American strains, so far from being killed by heating to 80 C. for one hour, will withstand much higher temperatures, some even resisting the temperature of boiling water for a consid-

<sup>1</sup> From *Journal Amer. Med. Assoc.*, December 13, 1919.

<sup>2</sup> Georgina S. Burke: "The Effect of Heat on the Spores of *Bacillus Botulinus*: Its Bearing on Home Canning Methods," Part 1, *J. A. M. A.*, 73: 88 (Jan. 11), 1919. "The Relation of Forage Poisoning to Botulism," editorial, *Ibid.*, 73: 611 (Aug. 23), 1919; "Spoiled Canned Food," 73: 914 (Sept. 20), 1919. Charles Thom, Ruth B. Edmondson and L. T. Giltner: "Botulism from Canned Asparagus," *Ibid.*, 73: 907 (Sept. 20), 1919. John Weinzirl: "Bacteriology of Canned Foods," abstr., *Ibid.*, 72: 1031 (April 5), 1919. "*Bacillus Botulinus* Poisoning in Detroit," *General News, Ibid.*, 73: 18 (Nov. 1), 1919.

<sup>3</sup> Georgina S. Burke: "Spoiled Canned Foods and Botulism," *J. A. M. A.*, 73: 1078 (Oct. 4), 1919. John Weinzirl: *Ibid.*, 73: 1789 (Dec. 6), 1919.



erable period. The history of the canned foods implicated in botulism poisoning shows that the spores of *B. botulinus* pass through the ordinary processes of household canning without destruction. It seems to be a fact that, as far as recorded cases go, only two or three instances of botulism have been traced to factory canned goods, as against a much larger number attributed to foods prepared in the household. Whether this difference is due to the superior germicidal efficiency of factory methods of heating or to the circumstance that spoiled or swelled canned goods are more likely to be eliminated in the course of ordinary trade procedures or to a combination of these factors cannot be definitely established at this time. It does not seem, however, that we are justified in asserting that a danger is entirely absent because it is exceedingly slight.

The main point of difference between the correspondents mentioned seems to hinge on the interpretation given by Weinzirl to the results of an extended bacterial examination of canned foods undertaken in the Department of Preventive Medicine at Harvard University.<sup>4</sup> The investigation forms part of a comprehensive study of canned foods, which is being carried out under the direction of Dr. M. J. Rosenau with the aid of a grant supplied by the National Cannery Association. The conclusion drawn by Weinzirl to which particular exception has been taken is that "food poisoning organisms, such as *B. botulinus*, *B. enteriditis*, etc., are not found in commercial canned foods." It is unfortunate that this matter was not allowed to rest in the form in which it appears in the summary of results. "Members of the paratyphoid-enteriditis group were not found, nor was *B. botulinus* ever isolated." This plain description of findings becomes transmogrified by Weinzirl in his "conclusions" into a general statement which would hardly be justified even by a more extensive investigation than that here under discussion, and which in its present form might lead to serious misinterpretation.

On the other hand, it must be admitted that a rather too positive tone pervades portions of Mrs. Burke's letter. It is hardly justifiable to insinuate, however vaguely, that a group of workers is influenced by any consideration other than the desire to seek the truth and find it.

It seems hardly fair or wise to cast discredit on the work of a

<sup>4</sup> John Weinzirl: "The Bacteriology of Canned Goods," *J. M. Research*, 39: 349 (Jan.), 1919.

group of scientific investigators, comprising some of the best-known names of the country, apparently on the ground that the money for the work has been provided by a commercial association. The word "commercial" is frequently used as a general term of opprobrium, but, as Roosevelt would have said, there is a "good" as well as a "bad" commercialism. It is not our understanding that money was given to Harvard University for the purpose of "exonerating" factory canned goods from any charge whatsoever, but simply for the purpose of discovering actual conditions and, so far as those conditions might be undesirable, of discovering and applying appropriate methods of improvement. It can hardly be assumed that the officials or any of the members of the National Canners Association would favor for an instant a plan to ignore or overlook any danger of botulism poisoning that might exist. Their interests, "commercial" as well as simply human, lie wholly in the direction of discovering what the danger is, how it arises, and how it can best be avoided or overcome. Denial or concealment is the last policy sound business judgment would dictate.

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#### REPORT OF THE INTERNATIONAL COMMITTEE ON ATOMIC WEIGHTS FOR 1919-20.\*

The last regular report of this committee, apart from an annual recommendation to continue the use of the table of atomic weights then presented, was published in 1916. The interruption in the series of reports was, of course, due to the World War, which created difficulties of a serious kind among all international organizations. Coöperation with Germany became impossible, partly because of the difficulty of correspondence, and partly because of the personal hostilities created by the conduct of the war. There was also an inevitable slackening of scientific activities, and this was well shown by the unusually small number of new researches in the field of atomic weights. Now that peace is in sight, it seems wise to resume the preparation of these reports, even though they may not be for some time quite so truly international as heretofore. The determinations published since the preparation of our last report may now be summarized as follows:

\* Reprinted from *Journal of the American Chemical Society*, Dec., 1919.

**HYDROGEN.**—A very thorough investigation by Burt and Edgar<sup>1</sup> on the volumetric composition of water has given the volume ratio of hydrogen to oxygen as 2.00288 : 1. From this value, taking the normal liter weights of oxygen and hydrogen as 1.42900 and 0.089873 Gm., respectively, the atomic weight of hydrogen becomes 1.00772, or, rounded off, 1.0077. Guye,<sup>2</sup> from a discussion of Burt and Edgar's data, accepts this value as lying between the two extremes of 1.00767 and 1.00773. If, however, instead of trusting to the densities of the gases and their physical constants exclusively, we take into account the admirable researches of Morley, Noyes and others, upon the synthesis and analysis of water,<sup>3</sup> the most probable general mean for the atomic weight of hydrogen becomes 1.0078, which differs from the volumetric value by only 1/10000; that is, the two distinct lines of attack upon the problem agree within the limits of actual uncertainty. For ordinary purposes the approximate value 1.008 is close enough. It must be remembered that the tables prepared by this committee are for the use, not so much for specialists, as for working chemists in general; and too much refinement will only lead to confusion. No determinations of these or any other constants can be absolute and final. All are subject to errors which may be reduced nearly, but not quite, to insignificance, but never eliminated entirely. For example, in the determination of atomic weights from gaseous densities it is not possible to guarantee the *absolute* purity of the gases, or to avoid errors in weighing, in reductions to a vacuum, or in the values given to the physical constants that are used in the final computations. Some of these errors may be so small as to be negligible, and in the aggregate they may tend either to reinforce or to compensate one another, but their extreme magnitude can be estimated with some approach to accuracy, and expressed by means of the usual  $\pm$  sign. At present an accuracy to within 1/10000 is the best we can expect to obtain.<sup>4</sup>

**CARBON.**—Two investigations on the atomic weight of carbon were reported from the Geneva laboratory in 1918. First, Stahr-

<sup>1</sup> *Phil. Trans.*, 216A: 393, 1916. This research was noted in the previous report for 1917. Its review by Guye renders its repetition desirable here.

<sup>2</sup> *J. chim. phys.*, 15: 208, 1917.

<sup>3</sup> Computation by F. W. C.

<sup>4</sup> For an elaborate discussion of sources of error in atomic weight determinations, see Guye and his colleagues (M. Germann, Moles and Renard) in *J. chim. phys.*, 14: 25, 195, 204, 1916; 15: 60, 360, 405, 1917; 16: 46, 1918.

foss<sup>5</sup> determined the density of acetylene, ethane and ethylene. Acetylene proved to be unsatisfactory, because of its tendency to polymerize. From ethane he obtained the value  $C = 12.006$ , and from ethylene  $C = 12.004$ . On account of some uncertainties in the reduction, he prefers, provisionally, the value  $C = 12.00$ .

Secondly, Batuecas<sup>6</sup> determined the density of ethane, and reduced his observations by 3 methods, giving  $C = 12.005$ ,  $11.999$  and  $11.996$ . The last two being concordant he regards as preferable, and their mean,  $C = 11.998$ , he adopts. It will be remembered that Richards and Hoover, by purely chemical methods, found  $C = 12.005$ ; and a later combination of all determinations published before 1918 gave the chairman of the committee the mean value  $C = 12.0025$ . For ordinary purposes the rounded-off value  $C = 12.00$  may be used, and is so given in the table.

BROMINE.—Three sets of determinations of the molecular weight of hydrogen bromide have been made in Guye's laboratory at Geneva, by Moles,<sup>7</sup> Reiman,<sup>8</sup> and Murray.<sup>9</sup> The acid used was prepared by several distinct methods, and all gave concordant results, which may be summarized as follows, when  $H = 1.0078$ :

	Mol. Wt. HBr.	At. Wt. Br.
Moles.....	80.9332	79.9254
Reiman.....	90.932	79.9242
Murray.....	80.930	79.9222

These values are wonderfully concordant and the variations are far within the allowable limits of experimental error. In a recent combination, by the chairman of this committee, of all the available data relative to the atomic weight of bromine, the value found was  $Br = 79.9228$ , in complete harmony with the Geneva determinations. For ordinary purposes the rounded-off figure 79.92 is enough.

BORON AND FLUORINE.—In a very original investigation Smith and Van Haagen<sup>10</sup> have simultaneously redetermined the atomic weights of boron and fluorine. Their starting point was anhydrous borax,

<sup>5</sup> *J. chim. phys.*, 16: 175, 1918.

<sup>6</sup> *Ibid.*, 16: 322, 1918.

<sup>7</sup> *Ibid.*, 14: 389, 1916. See review by Guye in the same number, p. 361.

<sup>8</sup> *Ibid.*, 15: 293, 1917.

<sup>9</sup> *Ibid.*, 15: 334, 1917. Reiman and Murray assume  $H = 1.008$ ; Moles prefers 1.0076.

<sup>10</sup> *Carnegie Inst. Pub.*, 1918, p. 267.

$\text{Na}_2\text{B}_4\text{O}_7$ , and their chief difficulty was in insuring the complete dehydration of that compound. The salt was then converted, in a series of successive experiments, into sodium sulphate, carbonate, nitrate, chloride and fluoride, which gave 8 independent values for boron ranging from 10.896 to 10.905, in mean, 10.900. This value was computed with  $\text{Na} = 22.997$ ,  $\text{Cl} = 35.457$ ,  $\text{S} = 32.064$ ,  $\text{N} = 14.010$  and  $\text{C} = 12.005$ . The authors finally discuss all previous determinations and show wherein they were affected by errors. The new value 10.900 should be adopted as the most probable.

In this research sodium fluoride was compared not only with borax but also with the sulphate, and the 8 values found ranged from 19.002 to 19.008, in mean 19.005. The rounded-off value  $F = 19.0$  may be retained for all practical purposes.

LEAD.—Oechsner de Coninck and Gérard<sup>11</sup> have attempted to determine the atomic weight of lead by calcination of the nitrate, and find  $\text{Pb} = 206.98$  when  $\text{N}_2\text{O}_5 = 108$ . This determination is evidently of no present value. With this exception the other recent researches relative to this constant have referred to isotopic lead, and the normal element is considered only in comparison with it. Richards and Wadsworth,<sup>12</sup> for instance, find for normal lead  $\text{Pb} = 107.183$ , and Richards and Hall<sup>13</sup> give  $\text{Pb} = 207.187$ , values slightly lower than the accepted 207.20 as determined by Baxter and Grover. Similar determinations by A. L. Davis<sup>14</sup> gave discordant results. As for isotopic lead its atomic weight is so variable as to show that it is nearly, if not always, a mixture of isotopes, and not a constant which can as yet be placed in the table. The values found have very great significance, but they are far from final.<sup>15</sup>

GALLIUM.—By the analysis of carefully purified gallium chloride, Richards, Craig and Sameshima<sup>16</sup> find  $\text{Ga} = 70.09$  and 70.11. These determinations, however, are only preliminary, but they justify the provisional adoption of the value 70.10. The original values given

<sup>11</sup> *Compt. rend.*, 163: 415, 1916.

<sup>12</sup> *J. Am. Chem. Soc.*, 38: 2613, 1916.

<sup>13</sup> *Ibid.*, 39: 537, 1917.

<sup>14</sup> *J. Phys. Chem.*, 22: 631, 1918.

<sup>15</sup> For discussions regarding the atomic weight of isotopic lead see the Presidential address of Richards before the American Association for the Advancement of Science, in December, 1918. Also F. W. Clarke, *Proc. Nat. Acad. Sci.*, 4: 181, 1918.

<sup>16</sup> *Proc. Nat. Acad. Sci.*, 4: 387, 1918.

by the determinations of Lecôq de Boisbaudran vary from 69.70 to 70.12, the last one being very near the new value.

ZIRCONIUM.—From the ratio between zirconium chloride and silver, Venable and Bell<sup>17</sup> find  $Zr = 91.76$ . Although this determination is regarded as preliminary, the authors, by pointing out sources of error in all previous values, believe the new one to be the most probable. It seems best, however, to await the complete investigation before changing the value heretofore accepted.

TIN.—Baxter and Starkweather,<sup>18</sup> by electrolyses of stannic chloride, find  $Sn = 118.703$  when  $Cl = 35.457$ . This is in complete agreement with Briscoe's determination,  $Sn = 118.698$ . The value 118.70 has already been adopted by the committee.

TELLURIUM.—Staehler and Tesch,<sup>19</sup> from careful syntheses of tellurium dioxide, find  $Te = 127.51$ , which is confirmatory of the accepted value 127.5.

YTTRIUM.—Hopkins and Balke,<sup>20</sup> by conversion of  $Yt_2O_3$  into  $Yt_2Cl_3$ , find  $Yt = 88.9$ . The ordinary sulphate method is shown to be inaccurate. In a later investigation Kremers and Hopkins<sup>21</sup> determined the ratio between yttrium chloride and silver, and found  $Yt = 89.33$ . Since this method is the most trustworthy, the value given by it should be adopted. The other sulphate determinations are questionable.

SAMARIUM.—The atomic weight of samarium has been determined by Stewart and James<sup>22</sup> from the ratio between the chloride and silver. The value found is 150.44, which is essentially that given in the table. No change is needed.

DYSPROSIUM.—Engle and Balke,<sup>23</sup> by conversion of the oxide into the chloride, found  $Dy = 164.228$ . Later, by the same method, Kremers, Hopkins and Engle<sup>24</sup> found  $Dy = 163.83$ . This discordance, like that already shown for yttrium, led the last-named chemists to determine the ratio between dysprosium chloride and silver, which gave 162.52. The earlier method is discredited and

<sup>17</sup> *J. Amer. Chem. Soc.*, 39: 1598, 1917.

<sup>18</sup> *Proc. Nat. Acad. Sci.*, 2: 718, 1916.

<sup>19</sup> *Z. anorg. allgem. Chem.*, 98: 1, 1916.

<sup>20</sup> *J. Am. Chem. Soc.*, 36: 2332, 1916.

<sup>21</sup> *Ibid.*, 41: 718, 1919.

<sup>22</sup> *J. Am. Chem. Soc.*, 39: 2605, 1917.

<sup>23</sup> *Ibid.*, 39: 67, 1917.

<sup>24</sup> *Ibid.*, 40: 598, 1918.

the last value, rounded to 162.5, seems to be the one best entitled to acceptance.

ERBIUM.—For this element, by the oxide-chloride method, Wichers, Hopkins and Balke<sup>25</sup> obtained values ranging from Er = 168.00 to 168.84. The method of determination is thus again shown to be untrustworthy.

THORIUM.—In a long series of concordant analyses of thorium bromide, Hönigschmid<sup>26</sup> finds Th = 232.152 from the silver ratio and 232.150 from the silver bromide ratio when Br = 79.916. The value Th = 232.15 should be adopted for general use. He also studied thoria from uranium ores, which contained ionium. For this mixture he obtained an atomic weight slightly in excess of 231.50. This may approximate to the unknown atomic weight of ionium.

URANIUM.—The later series of determinations of the atomic weight of uranium by Hönigschmid and Horovitz<sup>27</sup> was based like their earlier series upon analyses of the tetrabromide. Two sets of analyses were made, one upon a bromide which had been fused in bromine vapor, the other in nitrogen. The value obtained ranged from U = 238.04 to 238.16, the latter being in harmony with their former determinations. The rounded figure 238.2 is given in the table.

HELIUM.—Taylor,<sup>28</sup> using the microbalance for determining the density of helium, finds He = 4.0008. Guye,<sup>29</sup> in a recalculation of the data, finds He = 3.998. The value 4 should be retained.

ARGON.—From the density and compressibility of argon, Leduc<sup>30</sup> finds A = 39.91. He regards the second decimal as uncertain, and advises the adoption of the rounded value 39.9.

In the following table of atomic weights proposed for 1920, few changes have been made from the values given in the last preceding table. The new values are A = 39.9; B = 10.9; Ga = 70.1; Th = 232.15; and Yt = 89.33. In addition to these the atomic weight of nitrogen should be changed from 14.01 to the more precise value 14.008. The latter figure represents all the best determinations,

<sup>25</sup> *J. Amer. Chem. Soc.*, 40: 1615, 1918.

<sup>26</sup> *Z. Electrochem.*, 22: 18, 1916.

<sup>27</sup> *Monatsh.*, 37: 185, 1916.

<sup>28</sup> *Phys. Rev.*, 10: 653, 1917.

<sup>29</sup> *J. chim. phys.*, 16: 46, 1918.

<sup>30</sup> *Compt. rend.*, 167: 70, 1918.

## INTERNATIONAL ATOMIC WEIGHTS, 1920.

	Symbol.	Atomic Weight.		Symbol.	Atomic Weight.
Aluminum.....	Al	27.1	Molybdenum.....	Mo	96.0
Antimony.....	Sb	120.2	Neodymium.....	Nd	144.3
Argon.....	A	39.9	Neon.....	Ne	20.2
Arsenic.....	As	74.96	Nickel.....	Ni	58.68
Barium.....	Ba	137.37	Niton (radium emanation)Nt		222.4
Bismuth.....	Bi	208.0	Nitrogen.....	N	14.008
Boron.....	B	10.9	Osmium.....	Os	190.9
Bromine.....	Br	79.92	Oxygen.....	O	16.00
Cadmium.....	Cd	112.40	Palladium.....	Pd	106.7
Caesium.....	Cs	132.81	Phosphorus.....	P	31.04
Calcium.....	Ca	40.07	Platinum.....	Pt	195.2
Carbon.....	C	12.005	Potassium.....	K	39.10
Cerium.....	Ce	140.25	Praseodymium.....	Pr	140.9
Chlorine.....	Cl	35.46	Radium.....	Ra	226.0
Chromium.....	Cr	52.0	Rhodium.....	Rh	102.9
Cobalt.....	Co	58.97	Rubidium.....	Rb	85.45
Columbium.....	Cb	93.1	Ruthenium.....	Ru	101.7
Copper.....	Cu	63.57	Samarium.....	Sa	150.4
Dysprosium.....	Dy	162.5	Scandium.....	Sc	44.1
Erbium.....	Er	167.7	Selenium.....	Se	79.2
Europium.....	Eu	152.0	Silicon.....	Si	28.3
Fluorine.....	F	19.0	Silver.....	Ag	107.88
Gadolinium.....	Gd	157.3	Sodium.....	Na	23.00
Gallium.....	Ga	70.1	Strontium.....	Sr	87.63
Germanium.....	Ge	72.5	Sulphur.....	S	32.06
Glucinum.....	Gl	9.1	Tantalum.....	Ta	181.5
Gold.....	Au	197.2	Tellurium.....	Te	127.5
Helium.....	He	4.00	Terbium.....	Tb	159.2
Holmium.....	Ho	163.5	Thallium.....	Tl	204.0
Hydrogen.....	H	1.008	Thorium.....	Th	232.15
Indium.....	In	114.8	Thulium.....	Tm	168.5
Iodine.....	I	126.92	Tin.....	Sn	118.7
Iridium.....	Ir	193.1	Titanium.....	Ti	48.1
Iron.....	Fe	55.84	Tungsten.....	W	184.0
Krypton.....	Kr	82.92	Uranium.....	U	238.2
Lanthanum.....	La	139.0	Vanadium.....	V	51.0
Lead.....	Pb	207.20	Xenon.....	Xe	130.2
Lithium.....	Li	6.94	Ytterbium(Neoytterbium)Yb		173.5
Lutecium.....	Lu	175.0	Yttrium.....	Yt	89.33
Magnesium.....	Mg	24.32	Zinc.....	Zn	65.37
Manganese.....	Mn	54.93	Zirconium.....	Zr	90.6
Mercury.....	Hg	200.6			



and is probably correct to within 1 in the third decimal place. For so small a value the change is insignificant.

[Signed], F. W. CLARKE,  
T. E. THORPE,  
G. URBAIN.

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## OLIVE OIL SITUATION IN ITALY.<sup>1</sup>

By A. A. OSBORNE,

SECRETARY TO THE COMMERCIAL ATTACHÉ, ROME, AUG. 23, 1919.

Last year's total yield of olive oil in Italy, although it exceeded the average annual yield for the past ten years, was not sufficient to provide for the total yearly consumption, according to a communication to *Il Sole*. The monthly consumption of edible olive oil in Italy ranges at present from 120,000 to 130,000 quintals. This means that the average annual requirements amount to 1,500,000 quintals. The most favorable estimates of next year's production go no higher than 1,300,000 quintals.

The apparent deficiency of 200,000 quintals in olive oil production (obtained from the excess of requirements over production as they are both given above) must be made this year to supply oil to the redeemed territories, where the inhabitants have been almost without edible oils and fats during the war and are eager to secure them now in large quantities. The continued and prospective scarcity of butter likewise will result in a demand for oil to take its place.

The writer goes on to point out that a substantial portion of Italy's olive oil requirements must be met by importations. For imported olive oil, the market prices must naturally be paid, which are not subject to regulation by the Italian Government. The only price policies left open to the Government regarding this imported oil are two: (1) To sell the imported oil to the consumer at the domestic price, the Government bearing the loss; (2) to raise the fixed price of domestic oil so as to accord with the price paid for the imported oil.

<sup>1</sup> From *Commerce Reports*, Oct. 16, 1919.

GUM TRAGACANTH.<sup>1</sup>

In the course of a report furnished by the Revenue Commissioner in Mesopotamia it is stated that the most valuable of the gums collected is tragacanth, which is produced by tapping small shrubs which grow all over the mountains of Southern Persia, and from there through the entire mountainous region which runs northwest along the frontiers of Mesopotamia, comprising such areas as northern Arabistan, the Luristan-Pust-i-Kut country, and Kurdistan. The most important collecting center for Bagdad is Suleimanaya, the capital of the Suleimanaya district of Kurdistan, situated about 180 miles to the northeast of Bagdad. In this area there is a regular trade in this gum for the Bagdad market. The gum is called "Al-kitirah" in Arabic. The method of tapping the bushes is as follows: The Kurds first burn all the leaves off the bushes, then expose the roots, cut incisions in the roots, and leave for a week or so; they then return and collect the gum which exudes from the roots. The first tapping produces white gum of the best quality, second and subsequent tappings gums of yellow colors and inferior quality. Excessive tappings weaken, and may sometimes kill the bushes. The Kurds bring in the gum to Suleimanaya where it is bought by local merchants who export it to Bagdad on pack transport in caravans, and sell to Bagdad merchants. These merchants export to England and foreign countries. The local customs authorities levy a 12½ per cent. tax on the market value in Suleimanaya.

The northern mountainous Kurdish country in the Mosul Vilayet is a mass of mountains and valleys. The mountains are covered with scrub evergreen oak forest, and the higher hills and plateaux are full of these gum bushes. No organized trade, however, appears to exist, although Persian merchants are said to have come down off and on in the past to exploit these gums. The distance from the Mosul town to this gum-bearing country is from 50 to 100 miles. All transport at present is on pack animals, but three unmettaled roads up to the hill country have been constructed. The country is meanwhile wild and unsettled, but with the introduction of law and order, the opening up of the country by means of roads and the construction of a railway to Mosul, which means

<sup>1</sup> From *The Chemist and Druggist*, November 1, 1919.

direct rail from Mosul to Basrah, the exploitation of gums in this country should be possible in the near future. An article written in 1903 in a book about agriculture in the Bagdad Vilayet, states that the export from Bagdad in 1887 was 641,250 kilograms (= 130 tons) and in 1890 it had decreased to 39 tons.

A second kind of gum is produced from a large tree which grows throughout the part of Kurdistan now under British occupation. The tree grows to a great size, 50 feet high and up to 8 feet in girth. It is found scattered throughout the valleys only, especially near the villages in the forests. The tree produces edible fruits, sold for food and extraction of oil in Mosul, Bagdad, and all other local markets of any size in northern Mesopotamia, and also this gum, called "elk" (elch) in Arabic. The method of tapping this elch gum is by making long incisions in the trunks of the trees, placing some receptacle underneath to catch the exudation. A regular trade exists in the Suleimanaya district of Kurdistan, but there is none at all in the north of Kurdistan, which falls in the Mosul Vilayet, although "Button" trees abound in the valleys of that country. The bulk of this elch gum is exported direct from the Suleimanaya district by caravan to Aleppo, where it is used for sizing cloth. Some portion comes to Bagdad city, and there is no foreign export from Bagdad; it is all used locally for (a) sizing cloth, (b) in local medicines, (c) as a local chewing gum, (d) in the manufacture of arrack liquor from dates. The price of this gum in Bagdad at present is Re. 1.8.0 per lb. There is no doubt that very large amounts of this gum could be collected from the areas mentioned, under conditions similar to those already described for tragacanth.

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## A MODIFICATION OF THE PHENYLHYDRAZINE METHOD OF DETERMINING PENTOSANS.\*

BY PAUL MENAUL AND C. T. DOWELL.

Everyone who has made determinations of pentosans by the phloroglucinol method realizes that a shorter and less expensive method is very much needed. This is especially true at this time when it is almost, if not impossible, to buy phloroglucinol even at

\* Reprinted from *The Journal of Industrial and Engineering Chemistry*, November, 1919.

the high price asked for it. Our purpose in this short investigation was to try to overcome this difficulty by modifying the phenylhydrazine method so as to make it shorter and at the same time obtain results by this method which would agree with the provisional phloroglucinol method.

Recent investigations make it more and more evident that many compounds other than the pentoses and pentosans give furfural when they are distilled with hydrochloric or sulphuric acid, and hence neither the phloroglucinol method nor any other method of determining the furfural coming from such a distillation will enable one to say definitely that the original substance contained a certain per cent. of pentosans.

We thought it should be possible to precipitate the furfural with phenylhydrazine and determine the excess of phenylhydrazine in the filtrate by the use of some compound which would oxidize the phenylhydrazine. Tests were made using solutions of phenylhydrazine sulphate and iodine, potassium dichromate, ferric sulphate, sodium hypobromite and Fehling's solution. With the iodine almost theoretical results were obtained when a large excess of it was used. The amount of ferrous salt found was always less than the theoretical. No better results were obtained with the other oxidizing agents. These results are in harmony with what Chattaway<sup>1</sup> found in his work on the hydrazines. R. Adan<sup>2</sup> found that the reaction between phenylhydrazine, zinc and copper sulphate always gave less than the theoretical amount of nitrogen. He stated that secondary products such as chlorophenylhydrazine and diazo compounds were formed when hydrochloric acid was present. E. Ebler<sup>3</sup> found that a quantitative yield of nitrogen was obtained in the reaction between an ammoniacal solution of copper sulphate and hydrazine. We thought that this reaction might be quantitative for phenylhydrazine also if no chloride or other halogen ion was present in the solution to cause the side reactions found by Adan. The distillation, was therefore made using sulphuric instead of hydrochloric acid and using sodium sulphate instead of sodium chloride to lessen the solubility of the precipitate.<sup>4</sup> In the distillation the volume in

<sup>1</sup> *J. Chem. Soc.*, 91: 1323, 1907; 95: 1065, 1909.

<sup>2</sup> *Bull. soc. chim. Belg.*, 21: 211, 1907; abstracted in *J. Chem. Soc.*, [II] 91: 657, 1907.

<sup>3</sup> *Z. anorg. Chem.*, 47: 371, 1905; abstracted in *J. Chem. Soc.*, [II] 90: 53, 1906.

<sup>4</sup> Recommended in U. S. Department of Agriculture, Bureau of Chemistry, *Bulletin* 49.

the flask was kept practically constant by adding water as the distillation proceeded.

After the addition of the phenylhydrazine to an aliquot of the distillate the solution was stirred for the required time by bubbling carbon dioxide into it. An aliquot (50 Cc.) of the filtrate from the hydrazone was put by means of a dropping funnel into a 250 Cc. Fresenius nitrogen bulb,<sup>5</sup> which had been previously filled with a 10 per cent. solution of ammoniacal copper sulphate and heated to expel the air. A 100 Cc. burette was connected to the tube of the Fresenius bulb and a glass tube provided with a stopcock connected the neck of the bulb with a Schiff's nitrometer containing sulphuric acid. The aliquot of the filtrate was brought into the bulb through the dropping funnel by closing the cock leading to the nitrometer and lowering the burette. The bulb was then heated so as to keep the reaction mixture near the boiling point until the reaction was complete.

Results obtained, using the above method to determine the pentosans in three samples of grain sorghum which were cut at different stages of growth, are given in the table below. Results obtained by Mr. Freidemann of this laboratory using the same samples and the phloroglucinol method are given for comparison. Neither Mr. Freidemann nor Mr. Menaul knew what results the other had obtained until the work had been finished.

TABLE SHOWING WEIGHTS OF PENTOSANS IN ONE GRAM OF SORGHUM.

No.	Phloroglucinol Method. Gram.	Phenylhydrazine Method. Gram.
I.....	0.1790	0.1788
II.....	0.1523	0.1526
III.....	0.2149	0.2150

Other determinations showed that the addition of sodium sulphate to the distillate with the phenylhydrazine was not necessary. The same volume of nitrogen was obtained by taking two parts of the distillate to one of which sodium sulphate had been added and not to the other.

The time required to make a determination of the excess of phenylhydrazine in the filtrate is about 20 min. This method then makes it possible to use a much cheaper substance than phloroglu-

<sup>5</sup> See catalogue of Central Scientific Company, p. 371.

cinol and to make a determination of pentosans in a much shorter time.

OKLAHOMA AGRICULTURAL EXPERIMENT STATION,  
STILLWATER, OKLAHOMA.

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## NOTES ON ALUMINIUM FLARES.<sup>1</sup>

BY ERNEST H. BRITAIN.

The use of magnesium ribbon and powder in flashlight photography is familiar to every chemist, but it is not so generally known that aluminium is more frequently used in the various signal lights, rocket stars, ground flares, etc., which became so familiar during the great war. Aluminium is used in the form of fine powder similar to the aluminium bronze used in making aluminium paints, etc., and for pyrotechnic purposes is compounded with barium or potassium nitrate and other ingredients in varying proportions, according to the specific purpose for which the flare may be required. Sometimes a mixture of aluminium and magnesium is used, as in the "star compositions" used in signal rockets. The aluminium powder should be very fine, capable of passing through a 120-mesh sieve, and should be as free from oil, grease, or soap as possible. It must also be free from grit, sand, or other impurities. There are two kinds of aluminium powder on the market—a dull grey variety and a bright, lustrous, silvery kind (but every gradation between is also made). The lustrous kind is used for aluminium paints on account of this property, and its luster is due to the use of oil or grease in manufacture. This kind is not so suitable for pyrotechnical purposes as the dull grey, since it is more dangerous when compounded. Even dull aluminium powders frequently contain considerable percentages of oil, oil being used by the manufacturer as a safety precaution. The powdering of aluminium is a dangerous business, as spontaneous combustion is not infrequent, and with the intense heat of burning aluminium, to say nothing of the explosive violence of such conflagrations, any measure of precaution is welcomed by the manufacturer. The exact cause of these spontaneous ignitions is unknown, but the use of oil in powdering seems to prevent them to a considerable extent. Even then the mills are operated in the open, or only under rough sheds, and left unat-

<sup>1</sup> From *The Chemist and Druggist*, November 22, 1919.

tended while running for considerable periods, the progress being watched from a safe distance. The oil, which is often impure, is undesirable for flare purposes, as small percentages have a detrimental effect upon the brilliancy and vigor of the flare compositions, as well as introducing an additional element of risk into these explosive combinations. This applies more to aluminium than to magnesium, for paraffin wax can be, and is, used in considerable proportions in magnesium combinations. Paraffin wax does not introduce an element of risk here, but it undoubtedly has a greater retarding effect upon aluminium than on magnesium. A typical *star composition* is composed of:

Magnesium in powder (60 mesh).....	27 parts
Aluminium in powder (120 mesh).....	9 parts
Barium Nitrate (100 mesh).....	58 parts
Paraffin Wax.....	6 parts

The paraffin wax is melted and the aluminium and magnesium incorporated (away from any naked lights). The mixture should be maintained at about 70° C. till the metallic powder is thoroughly coated with the melted wax. Allow to cool, pass through a sieve, and then mix with the barium nitrate. The barium nitrate must be anhydrous and in fine powder. The whole should be sifted to ensure uniformity. The composition is then pressed into suitable containers, with priming and quick-match for ignition. For use as a *ground flare* a short length of ordinary rolled cardboard tube plugged at one end with clay will do quite well. The priming may be:

Sulphur.....	2 parts
Saltpetre.....	6 parts
Orpiment (or black Antimony).....	1 part
made into a paste with shellac solution.	

Another formula, used as a *ground light*, is as follows:

Barium Nitrate.....	3,000 grams
Aluminium (120 mesh).....	800 grams
Aluminium (60 mesh).....	400 grams
Castor Oil.....	60 grams

An excellent *flare*, fairly slow in burning, but giving a good light, and used in illuminating enemy working parties, is composed of:

Barium Nitrate.....	55 parts
Aluminium.....	20 parts
Potassium Nitrate.....	4 parts
Sulphur.....	20 parts
Powdered Shellac.....	1 part

If the shellac is increased to 3 per cent. or 5 per cent., the flare is slower in burning, but loses its brilliancy. In general, the brilliancy and fierceness of burning increases with the percentage of aluminium up to fifty, and is decreased by the addition of such substances as sulphur, or shellac, or borax, or castor oil. The fiercest and brightest aluminium combination consists of:

Aluminium in fine powder.....	1 part
Barium Nitrate.....	1 part

If this mixture is packed in an iron tube, say  $\frac{3}{4}$  in. bore, and with walls of  $\frac{1}{16}$  in. thickness of metal, it will melt and burn the iron like so much paper. As combustion proceeds down the tube the walls fuse and molten globules of white-hot metal fall to the ground. If a tube of any considerable length be used it should be stuck in the ground at an angle, as the molten metal falling vertically may fire the composition at the base of the tube and cause a powerful explosion. Though the proportions in the above formula give an excess of aluminium over what would be necessary for chemical equivalents, the mixture is much fiercer and brighter.

Aluminium.....	1 part
Barium Nitrate.....	3 parts

gives a mixture which more nearly corresponds to molecular equivalents.

Potassium nitrate may be used instead of barium nitrate in these combinations. The burning is slightly slower, and the light of a different character, as may be imagined, the lilac potassium flame being different from the green of barium. In the same way the mixing of borax in a flare gives the yellow sodium flame, but the intensity of the aluminium flame makes these colored effects only slight variations from the characteristic dazzling "whiteness." Aluminium flares are not quite so "white" as magnesium ones, but the heat of combustion is much higher. Simple mixtures of aluminium powder and barium nitrate in dry powders do not bind well



for packing in containers or tubes, and tight packing is essential to regularity and length of burning. Consequently such substances as boiled or castor oil, paraffin wax, shellac, borax, bird-lime and even small percentages of sodium nitrate (which is deliquescent), are incorporated, and allow of more compact packing. These flare combinations will all stand quite a lot of direct pressure, but glancing blows or friction should be avoided. They are less sensitive than gunpowder, but must nevertheless be looked upon as explosives, and though they burn safely enough with free access to the air, under conditions of confinement they are liable to violent explosion.

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### THE SANTONIN MARKET.<sup>1</sup>

The recent enormous advance in the price of this vermifuge, hitherto regarded as indispensable, took by surprise even those who have been closely following the upward movements from time to time. In view, however, of the fact that the sole source of supply is Eastern Turkestan, which part of the world would appear to have come wholly under the control of the Bolsheviks, the successive advances in price which had hitherto taken place can hardly be said to have come as a surprise. But the last advance was staggering. Fifty pounds sterling per kilo. (1s. per gram), or nearly twenty-two pounds fifteen shillings (more exactly, 22£ 13s. 6d.) per lb., is now the price of a drug which between twenty and thirty years ago was obtainable in cwt. lots at four shillings (4s.) per lb. This lowest price was the result of competition between the various producers of santonin prior to the amalgamation of the various factories in Turkestan, and consequent total elimination of competition. It is stated that the immediate cause of this late enormous advance has been, firstly, the total cessation of fresh imports, and, secondly, the gradual diminution of stock in London, there being, so far as is known, no stock held in any other part of the world which could become available in the direction of averting the threatened famine. The quite small stock of santonin held here is in the hands of the Eastern and Russian Trading Co., Ltd., which company, it is understood, is the sole representative of the combined Turkestan factories, and will, when matters have settled down and have again

<sup>1</sup> From *The Chemist and Druggist*, November 15, 1919.

become more or less normal, handle the entire production of santonin of the factories, which factories will in turn practically control the sale and production of santonin for the whole world. The reason why the Turkestan factories exercise control, and will continue to do so, is found in the fact that the plant, *Artemisia maritima*, from the unopened flower buds (erroneously called wormseed) of which the article is produced, while growing freely in many parts of the world (it is said to be found fairly abundantly on the Essex saltings), only yield santonin in paying quantity when grown on the salt steppes of Turkestan. Of course, it is not impossible, although it is to be hoped not very probable, that the Turkestan factories are hopelessly ruined, in which case the prospects for the future supply would appear to be very remote. It is true that santonin was formerly manufactured in Europe before the Turkestan factories were built, the so-called wormseed traveling, it is understood, a couple of thousand miles by bullock cart before it reached railhead, thence by rail to a Baltic port, to Hamburg, whence it was sent to the one, two, or three makers on the Continent, the drug not having, we believe, been produced on a commercial scale, or in fact at all, in this country. In normal times the santonin produced by the Turkestan factories would also travel by the above route, at least as far as a Baltic port. Of course, with affairs in their present condition in Russia all this is a thing of the past. Firstly, the two Turkestan factories are not working; in fact, it is not known really for certain whether they are actually still in existence. Secondly, as far as the latest news—dating, we believe, from late in the year 1917—there was practically no stocks of manufactured santonin left at the factories which do not appear to have been working since that date. It is believed possible that the Bolsheviks, when they obtained control of the districts in which the factories are situated, may have been stolen and hidden a thousand kilograms or so of santonin; this is, however, not known for certain, while it is equally uncertain whether such 1,000 kilos, even if the Bolsheviks did secure same is still in existence. The primary cause of the late enormous advance in the price of santonin appears to have been the definite and total disappearance of a parcel of forty-nine cases, each containing 50 kilos, which were dispatched from the works some time in 1917 via the Siberian Railway to Vladivostok, for shipment thence to Europe. This little lot of nearly two and a half tons, worth at least the present highly inflated price about 120,000 £,

appears to have absolutely disappeared en route. In all probability it was stolen, and the lot is quite possibly still in existence somewhere. To add to the stringency of the situation, it is reported that there are urgent inquiries for santonin on the market from the United States, and if these had led to business the present quite limited stock in the hands of the sole importers would be exhausted. The sole hope in the situation is practically confined to the fact that the present enormous cost will quite certainly so reduce the actual consuming demand that the very meagre stock available may at a pinch last out until matters change and fresh supplies come in, but this is indeed a vague hope. Also, what applies to the importation of santonin also equally applies to the importation of the so-called wormseed, in view of the enormously large bulk of such wormseed. The Eastern and Russian Trading Co., Ltd., state that they have also a certain, not very large quantity of wormseed in stock, but they also state that the quality is not quite suited to the manufacture of santonin, this being probably due to the comparatively low yield of the drug, good manufacturing wormseed yielding about 2 per cent. of santonin. Apart from this fact, the difficulty of manufacture would probably arise, it being open to question whether any of our fine chemical makers would be prepared to undertake the production of santonin on a commercial scale, even assuming that satisfactory raw material were available. Perhaps some French manufacturer might be willing to oblige, but even then the question of suitable raw material would still be the crux. As far as can be judged from the foregoing, the enormous price of santonin would appear likely to be maintained for the present and in the near future, at any rate.

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### CALCIUM CREOSOTE.<sup>1</sup>

Under the name of *Calcreose* has been introduced a dark brown powder, partially soluble in water, and said to contain in loose chemical combination equal weights of creosote and lime. Its therapeutic effect is similar to that of creosote, while it does not produce gastric irritation. Dose, 0.25 to 1.0 Gm. (4 to 16 grains) every two to four hours (see *The Prescriber*, 1918, p. 47).

A formula for the preparation of a similar compound in liquid form is given in the *Pharmaceutical Journal*. One part by weight of

<sup>1</sup> From *The Prescriber*, December, 1919.

creosote is mixed in a percolator with four or five parts of freshly slaked lime. After the mixture has cooled, water is poured on and allowed to run through slowly until the sp. gr. drops below 1.010, when a fresh portion of creosote is added and the process repeated. The resulting solution of calcium creosote is a reddish yellow liquid, becoming brown on keeping and depositing a precipitate of calcium carbonate on exposure. It has the odor of creosote, a sharp, peppery taste, an alkaline reaction, and marked antiseptic properties. It contains the equivalent of about 3 minims of creosote in each fluid drachm, and affords a means for the administration of creosote in relatively large doses without, as a rule, producing intolerance.

#### GUAIACOL IODIDE: AN ORGANIC IODINE COMPOUND.<sup>1</sup>

A combination of guaiacol and iodine is recommended by J. Maberly (*Med. Jour. S. Africa*, 14: 367 (Feb.), 1919) as a convenient means for the administration of iodine in organic combination. This is prepared according to the following formula:

Guaiacol, pure.....	1 minim.
Solution of Iodine (12½ grs. in one ounce S. V. R.).....	1 minim.
Rectified Spirit.....	20 minims.
Distilled Water.....	to 60 minims.

The drugs are mixed in the order given above, a slight rise of temperature taking place on the addition of the water. The free iodine disappears and a stable compound is formed in which the iodine, or a portion of it, replaces hydrogen in the guaiacol. One drachm of guaiacol-iodide solution prepared as above represents 0.026 grain (about 1/40 grain) of iodine.

The dose of this solution is one drachm, mixed with an equal quantity of simple syrup and two drachms or more of water. Maberly recommends its use in all cases in which iodine internally is indicated, such as glandular enlargements, etc. The dose is suitably reduced in the case of children.

<sup>1</sup> From *The Prescriber*, December, 1919.

## PRELIMINARY REPORT ON PRODUCTION AND STOCKS OF NAVAL STORES.

The following preliminary report on the production and stocks of naval stores is made by the Bureau of Chemistry, United States Department of Agriculture:

### PRODUCTION.

The statistics compiled by the Bureau of Chemistry from individual reports from producers show that there was made during the first half of the present season, up to August 1, about 163,000 casks of turpentine and 491,000 round barrels of rosin (500-pound barrels). Producers' estimates for the balance of the season from August 1 to the close of operations, indicate that about 174,000 casks of turpentine and 547,000 round barrels of rosin will be made during this period, indicating a total production for the season of 337,000 casks of turpentine and 1,038,000 barrels of rosin. This does not include wood turpentine, wood rosin or rosin reclaimed from batting dross. The actual figures are as follows:

On Hand at Stills April 1, 1919.		Made This Year up to Aug. 1, 1919.		Estimated Production Balance of season.		On Hand at Stills Aug. 1, 1919.	
Turp.	Rosin.	Turp.	Rosin.	Turp.	Rosin.	Turp.	Rosin.
24,050	130,035	163,301	491,110	174,433	547,165	19,364	115,702

A comparison of these figures with the reports issued as of August 1, 1918, and March 31, 1919, show that the production during the first half of the present season was approximately the same as for the same period in 1918. More trees are being worked this year than last year, but unseasonable weather conditions and excessive rains throughout the turpentine-producing sections kept production down during the early part of the season. The weather has been very favorable since September 1, and it is believed that the production for the latter half of the season will be greater than shown by the estimates, indicating that, for the entire season, the production will be at least equal to, and possibly slightly greater than that of the 1918-1919 season.

### QUANTITIES AT STILLs.

The quantity of turpentine and rosin on hand at the stills on August 1, 1919, was considerably less than on the same date last year, as shown by the following figures:

	Turpentine.	Rosin.
On Hand at Stills Aug. 1, 1918.....	59,000 casks	170,000 bbls.
On Hand at Stills Aug. 1, 1919.....	19,000 casks	115,000 bbls.

This decrease is undoubtedly due to the higher prices prevailing this year and to the increase of exports.

The stocks of turpentine at the stills decreased 16,000 barrels, and rosin decreased 45,000 barrels from March 1, 1919, to April 1, 1919, the last month of the naval stores year, when practically nothing was made. This decrease is shown by the following figures:

	Turpentine.	Rosin.
On Hand at Stills March 1, 1919.....	40,000 casks	175,000 bbls.
On Hand at Stills April 1, 1919.....	24,000 casks	130,000 bbls.

Production has been greater in Georgia and Florida this year, up to August 1, than it was last year. In the other states it has been less this year than it was last. This, together with the fact that large quantities of old turpentine and rosin which had been made during previous seasons and tanked and stored at the stills, have been shipped into the three main eastern ports this year, probably accounts for the considerable increase in receipts reported at Savannah, Jacksonville and Pensacola, compared with last year. This is especially true of turpentine.

#### STOCKS IN HANDS OF CONSUMING INDUSTRIES ON AUGUST 1, 1919.

The total stocks of turpentine and rosin in the hands of the paper, paper size, paint and varnish, soap, greases and lubricants, shoe polish and leather dressings, rosin oil and pitch, printing ink, sealing wax and insulating materials, soldering flux, matches and woodenware, fly paper, linoleum, automobiles, buggies and wagons, and foundries and foundry supply industries on August 1, 1919, were approximately as follows:

	Turpentine.	Rosin.
On Hand August 1, 1919.....	20,500 casks	182,000 bbls.*
On Hand April 1, 1919.....	28,500 casks	203,000 bbls.
Decrease.....	8,000 casks	21,000 bbls.

Many producers and consumers have not furnished promptly the information on their production and stocks. Some have ignored repeated requests. In every case where producer or consumer has

either failed or deliberately refused to send in the reports, conservative individual estimates on such delinquent concerns have been made. These estimates, which are included in the figures given, comprise only 6 per cent. of the total production shown. About 10 per cent. of the total turpentine stocks and about 7 per cent. of the total rosin stocks shown as in the hands of consumers are estimates on such individual concerns from which no information was received.

The value of these estimates to the individual concern and to the entire consuming or producing industry depends on their accuracy and prompt issue. It was hoped to publish the figures several months ago, but their issue was held up by lack of coöperation on the part of certain producers and consumers. It is hoped that in the future a more willing coöperation on the part of producers and consumers may be secured, to the mutual welfare of the interests of both. However, the failure of a small percentage of producers or consumers to submit their data will not prevent the publication of these statistics, but only serve to delay their issue, as estimates must be resorted to in every such case.

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## CURRENT LITERATURE.

### SCIENTIFIC AND TECHNICAL ABSTRACTS.

ESTIMATION OF ARSENIC IN SUBSTITUTED PHENYLARSINIC ACIDS AND THEIR REDUCTION PRODUCTS.—R. G. Fargher (*J. Chem. Soc.*, 1919, pp. 115-116, 982-992).—Ewins (*Analyst*, 42: 50, 1917) considers that the method devised by Lehmann (*Apoth. Zeit.*, 27: 545, 1912; *Analyst*, 37: 415, 1912) for the estimation of arsenic in salvarsan and neosalvarsan, while applicable to some derivatives, fails entirely in many cases, owing to the fact that the preliminary treatment with sulphuric acid and permanganate fails to bring about complete oxidation. It has now been found possible by the use of the modification described below to extend this estimation to many substituted phenylarsinic acids containing nitro-, amino-, hydroxy-, methoxy-, bromo-, and other groups. Some of the powdered substance (0.2 Gm.) is weighed and intimately mixed in a 250 Cc. flask with 1 Gm. of potassium permanganate. Five Cc. of 50 per cent. sulphuric acid are added, followed by a further 10 Cc.

of concentrated sulphuric acid when the first reaction has ended. After a few minutes, 10 Cc. of water are added, and the mixture is heated for half an hour to gentle boiling, precautions being taken against loss by spraying. The manganese dioxide is then removed by a slight excess of hydrogen peroxide, 30 Cc. of water are added, and the solution is again boiled for ten minutes, after which a dilute solution of potassium permanganate is added drop by drop until a faint, permanent pink tinge is obtained. This is discharged by the addition of a drop of dilute solution of oxalic acid. The solution is then cooled, 2.5 Gm. of potassium iodide are added, the whole being allowed to remain for an hour, and the liberated iodine titrated by means of thiosulphate. A blank experiment should be carried out alongside each estimation, and the final reading corrected accordingly. The following are examples of the results obtained:

Substance.	Found.		As.	Calc.
3-Nitro-4-hydroxyphenylarsinic Acid.....	28.4,	28.4		28.5
<i>p</i> -Aminophenylarsinic Acid.....	34.5,	34.5		34.6
1 : 2-Dihydrobenzoxazolone-4-arsinic Acid.....		28.6		28.9
3-Nitro-4-aminophenylarsinic Acid.....	28.9,	28.8		28.6
3 : 3'-Dinitro-4 : 4'-dihydroxydiphenylarsinic Acid....	19.6,	19.5		19.5
<i>p</i> -Bromophenylarsinic Acid.....		26.5		26.7

(From *The Analyst*, November, 1919.)

ANALYSIS OF VASELINE.—G. Armanni and A. G. Rodano (*Annali chim. applic.*, 12: 50-51, 1919).—A method of distinguishing between natural and artificial vaseline has been based upon the different solubilities of the two substances in a mixture of benzene and absolute alcohol (1 : 1). One part of the vaseline is dissolved in 20 parts of the hot solvent, and the solution allowed to stand for twenty-four hours in a cold place. If the vaseline be natural, there will only be a slight oily deposit, while artificial vaseline yields a flocculent or crystalline deposit resembling paraffin wax. In the case of mixtures the amount of precipitate is proportional to the quantity of artificial vaseline present, and the method will detect less than 20 per cent. of the latter. (From *The Analyst*, November, 1919.)

*Microscopic Diagnosis of Amebic Dysentery.*—For the fixation and staining of amebas, motile and encysted, Haig makes thin smears from the fresh stool, selecting, where present, a portion containing mucus and blood, on cover slips, and floated, without



drying, smear downward, on the following fixing solution: corrosive sublimate (saturated aqueous solution), 2 parts; absolute alcohol, 1 part. Fixation is complete in about thirty minutes. The smears are then placed film upward in iodized alcohol in order to remove the last traces of sublimate, washed in distilled water and then stained as follows: (1) Soak for several hours in a 4 per cent. solution of iron alum (made with violet crystals); (2) wash in distilled water; (3) stain in Heidenhain's hematoxylin for several hours (or over night); (4) wash in distilled water; (5) place in 1 per cent. iron-alum solution until decolorization has reached a satisfactory stage; (6) wash in distilled water and counter stain with 5 per cent. aqueous eosin solution; dehydrate through the alcohols, clear in xylol, and mount on a slide in Canada balsam. (*Lancet*, London; through *Jour. Amer. Med. Assoc.*, Dec. 6, 1919.)

THE ROMANOWSKY STAIN.—Romanese has worked out, he says, a simple and reliable substitute for the Giemsa method. The results seem to be the same with it as with the original Giemsa fluid, while the ingredients are inexpensive and always at hand. He dissolves 0.75 Gm. methylene blue in 50 Cc. of 95 per cent. alcohol and 50 Cc. of glycerin, and adds 3 Cc. of a 10 per cent. solution of sodium carbonate in distilled water, and boils for fifteen minutes. Then he adds 35 Cc. of a 1 per cent. alcoholic solution of eosin and boils fifteen minutes. It is then removed from the fire and alcohol is added to bring the total amount to 100 Cc. It is then set aside, covered closely, for a week. (From *Jour. Amer. Med. Assoc.*, October 11, 1919.)

FORMIC ACID IN THE COMMON NETTLE.—It is commonly stated in text books that formic acid occurs in the stinging hairs of the common nettle (*Urtica dioica*), but there is no satisfactory proof of the statement. When nettles are cut up and distilled with water the reactions for formic acid in the distillate are obtained, but it is now known that various parts of plants yield formic acid when treated in this way; therefore, it is not certain that the formic acid comes from the stinging hairs of the nettles; it may be derived from the general plant tissues. One of the chief chemical reactions of formic acid is its power of reducing salts of silver and mercury, but that is not necessarily conclusive proof in this case. The author appears to have settled the point definitely. By pressing the leaves of grow-

ing nettles between dry filter papers impregnated with barium carbonate the contents of the hairs are absorbed without contamination from juices from any other part of the plant. On appropriate treatment the product yielded barium and lead salts, which were crystalline on glass slides, and the two formates were identified under the microscope. Another question is whether or not formic acid is the main cause of the intense irritation produced by nettle stings; the active irritant is regarded by one investigator as being probably due to an enzyme and not to formic acid. (L. Dobbin, *Proc. Roy. Soc. Edin.*, II, No. 11; through *Nature*, September 18, 1919, p. 64; through *The Pharm. Jour. and Pharmacist*, Oct. 11, 1919.)

**TUBERCULOSIS INFECTION.**—Calmette (*Ann. Inst. Pasteur*, 1919, pp. 60-68) has established that many kinds of bacteria circulating in the blood are eliminated by the intestine; the bacillus of tuberculosis in particular is taken up by the liver and emptied into the intestine with the bile. Recent experiments have shown that tuberculosis is spread among cattle by the excreta, and this explains infection occurring in stables, and also the presence of tuberculosis bacilli in milk, even that from healthy cows. This fact also draws attention to the spread of tuberculosis through vegetables, due to contamination with tuberculous manure, and its propagation on farms and in rural districts. (From *The Chemist and Druggist*, October 18, 1919.)

**DETERMINATION OF GLYCYRRHIZIN.**—Dissolve 3 Gm. of ext. glycyrrhizae dried at 100° in 30 Cc. of water containing 5 drops of solution of ammonia, and filter. To 20 Cc. of filtrate add 2.5 Cc. of sulphuric acid and allow to stand for twenty-four hours. Decant the limpid liquid upon a filter, wash the residue with a total of 30 Cc. of water, filter and reject the washings. Dissolve the residue with 1 to 2 Cc. of solution of ammonia, pass the solution through the filter, and wash with 10 Cc. of water containing 5 drops of solution of ammonia until the washings are colorless. Evaporate the solution on a water bath and dry at 100°. Add 0.04 Gm. per 40 Cc. of washings and calculate the percentage. (Astruc and Pichard, *J. pharm. chim.*, 18: 289-90; through *The Chemist and Druggist*, Oct. 18, 1919.)

**RAPID DIAGNOSIS OF DIPHTHERIA BACILLI.**—Debré and Letulle expatiate on the differential importance of Babes' polar granules,

shown up by double staining, in true diphtheria bacilli. Their two years of experience with this method of differentiation has confirmed its precision and reliability. The pseudodiphtheria bacilli never show these granulations at the poles when stained by the technic described, which is a modification of Neisser's first method. The specimen is incubated at 55° C. for twenty hours and each loop of the culture is spread on two slides. One slide is treated with the Gram, the other after fixation by heat is covered with a solution made by dissolving 1 Gm. of methylene blue in 20 Cc. of 95 per cent. alcohol, and adding 950 Cc. of distilled water and 50 Cc. of glacial acetic acid. The smear covered with this solution is heated until it begins to steam. It is then heated a second time, and is then left in contact for five minutes. It is then rinsed rapidly with distilled water and covered with the second stain for ten or twelve seconds and rinsed quickly in distilled water. This second solution is made by dissolving 5.50 Gm. vesuvine in 250 Cc. of boiling distilled water, filtering while still boiling. The granules clustered at the poles of the bacilli, or only in some of them, show up a black oval, larger than the body of the bacillus. In their 800 tests they never found these polar granulated bacilli except with true diphtheria and they always found them then. They warn that one other bacillus may present these granulations, *Bacillus cutis-commune*. But they never found this in the throat in any of their tests. It differs from the diphtheria bacillus further in attacking saccharose. In case of diphtheric lesions elsewhere than in the throat, it might be advisable to test a loop on a sweetened litmus culture medium to exclude this bacillus. (From *Jour. Amer. Med. Assoc.*, Oct. 25, 1919.)

PRESENCE OF ACONITIC ACID IN SUGAR-CANE JUICE, AND NEW REACTION FOR THE DETECTION OF THE ACID.—C. S. Taylor (*J. Chem. Soc.*, 1919, 115, 886-889).—The presence of aconitic acid in sugar-cane juice was inferred by Behr (*Ber.*, 1877, 10, 351) but not conclusively proved. In the author's experiments aconitic acid was isolated from both healthy and diseased sugar cane, though it could not be obtained in crystalline condition from the latter. It is present in the form of a salt and not in the free state in the cane juice. In addition to the usual qualitative test it was found that aconitic acid when treated with acetic anhydride gives a pink coloration, which changes rapidly to deep red and then to magenta. On heating the mixture a bluish green liquid is obtained, which becomes

brown and almost opaque. The magenta liquid apparently consisted of two colored substances, a red compound soluble in water, and a blue compound readily soluble in ether, but both were exceedingly unstable and were rapidly decomposed by water, acids or alkalis. Apparently the color reaction is due to condensation of the carboxyl groups of the acid, with possibly elimination of water or addition of acetic anhydride. Applied as a test the reaction is capable of detecting 0.01 Mgm. of aconitic acid. None of the other acids in sugar-cane juice give the reaction, but citric acid may be detected by melting it in a test-tube, when traces of aconitic acid are produced, which then react with the acetic anhydride. (From *The Analyst*, Sept., 1919.)

ESTIMATION OF LACTIC ACID BY OXIDATION.—O. Schuppli (*Trav. Chim. Aliment. Suisse de Hyg. Pub.*, 1919, p. 44; *Ann. Chim. anal. Appl.*, 1: 222, 1919).—Szeberenyi has devised a method of estimating lactic acid by oxidizing it by chromic acid into acetic acid, carbon dioxide and water, distilling the acetic acid in a current of steam, and titrating the distillate with standard alkali solution. Other organic acids, including malic, tartaric and oxalic acids, are completely oxidized to carbon dioxide and water. In test experiments it was found that 97 per cent. of lactic acid was oxidized into acetic acid, carbon dioxide and water, and 3 per cent. completely oxidized to carbon dioxide and water. The author finds that this method gives satisfactory results with solutions of pure organic acids, but that when applied to wines it gives higher results than those obtained with Möslinger's method, owing to some of the other constituents undergoing incomplete oxidation, and yielding volatile acids. This was confirmed by experiments with cane sugar. (From *The Analyst*, Sept., 1919.)

LOROGLOSSIN, A NEW GLUCOSIDE IN LOROGLOSSUM HIRCINUM.—The biochemical method has given the authors indication of the presence of one or more glucosides in the aerial organs of all the native French orchids investigated. These included members of the genera *Aceras*, *Cephalanthera*, *Epipactis*, *Limodorum*, *Neottia*, *Platanthera*, *Ophrys*, *Orchis* and *Loroglossum*. A considerable quantity of *Loroglossum hircinum* was cultivated before the war, but the investigation of the material has been possible only recently. It has yielded a new *B*-glucoside, loroglossin, crystallizing in colorless,

odorless, very bitter, long needles; melting at  $137^{\circ}$  Corr.;  $[\alpha]_D$   $42.97^{\circ}$ . It is very soluble in water and in alcohol, sparingly soluble in acetone and in acetic ether. It does not reduce Fehling's reagent until hydrolyzed. This occurs when it is heated with dilute sulphuric acid and on contact with emulsin. The glucoside is accompanied in the plant by a considerable amount of glucose. The method by which it is separated is fully described. (E. Bourquelot and M. Bridel, *J. pharm. chim.*, 20: 81, 118, 1919; from *The Pharm. Jour. and Pharmacist*, Sept. 13, 1919.)

**SUBSTITUTE FOR SENNA LEAVES.**—Since the beginning of 1917 large quantities of so-called Palthe senna leaves have been imported into Germany from Switzerland. They have been identified as the leaves of *Cassia auriculata* L., and are readily distinguished from senna leaves by the rounded and not tapering apex. It is remarkable that they contain no oxymethylantraquinones and are free from laxative action. With Bornträger's reaction (shaking an infusion with petroleum benzine, separating and shaking the benzine with ammonia) a yellow coloration of the ammonia is produced, whereas with genuine senna leaves a rose color is obtained. (*Pharm. Ztg.*, 64: 242; from *The Pharm. Jour. and Pharmacist*, Sept. 6, 1919.)

**MICROSCOPICAL DETECTION OF RHAPONTIC RHUBARB.**—Mount a little of the powdered drug in water, wash three times by irrigation with more water, finally removing as much of the water as possible; then allow a mixture of 100 parts of 50 per cent. aqueous solution of potash with 5 parts of 100 volume perhydrol to flow on, and allow the preparation to stand for thirty minutes. Particles of the rhapontic powder will then have assumed an intense blue color, apparently due to a granular precipitate, while the particles of other rhubarbs are colorless, or orange-rose, or quite exceptionally reddish violet, but never blue and granular.—C. Winimer (*Pharm. Post*; through *Pharm. Ztg.*, 64: 348; through *The Pharm. Jour. and Pharmacist*, Sept. 6, 1919.)

**STAIN FOR TUBERCLE BACILLI.**—Gasbarrini has long contended that the acids used to decolor the bacilli with the usual technic are too powerful and detract from the effect. To avoid this he uses methylene blue in excess in a solution of 40 Cc. lactic acid in 160 Cc. distilled water, and adds to this at the time of using four parts of

alcohol (95°). This both decolors and recolors at the same time, with the finest and most constant results. It has shown up tubercle bacilli in sputum, urine and stools when the Ziehl gave negative findings, and the accuracy of the lactic acid method was confirmed by the course of the cases. The non-acid resisting bacilli can be differentiated more readily, and the whole procedure takes less time than the ordinary technic. (From *Jour. Amer. Med. Assoc.*, October 11, 1919.)

INSECTICIDAL PRINCIPLE.—This principle in *Chrysanthemum cinerariaefolium*, termed pyrethron by Sato, was found by Yamamoto (*Jour. Tokyo Chem. Soc.*, 40, 1919) to be present principally in the ovary of the flower, particularly abundant during the blooming period, while the other parts of the flower contained very little. Pyrethron is an almost neutral mixture, very sensitive to heat and air. On hydrolysis it yields two alcohols,  $C_{21}H_{34}O$  and  $C_{27}H_{46}O$ , one liquid fatty acid, palmitic acid and possibly another solid fatty acid. In a concentration above 0.077 per cent. pyrethron checks bacterial growth. Its saponification number is 216, iodine number 116. (From *The Chemist and Druggist*, October 4, 1919.)

RAPID DETERMINATION OF HYDROGEN ION CONCENTRATIONS.—A new apparatus for determining the dilution of hydrogen ion in bacterial cultures and other fluids is described by Jones. As compared with the colorimetric method, the apparatus here described has wider application, is more accurate, less cumbersome and only slightly less rapid. The hydrogen electrode vessel described was designed with two objects, chiefly, in mind: (1) to provide a vessel accurate at least to 0.01 pH, and (2) to provide a vessel giving rapid saturation with hydrogen gas, and yet one which is easily constructed. A rapid and labor-saving technic combining the indicator, and the gas-chain methods is described, which obviates the difficult task of preparing standard solution for the former methods, and of making needless repetitions by the latter.—(From *Jour. Amer. Med. Assoc.*, Sept. 27, 1919.)

#### MEDICAL AND PHARMACEUTICAL NOTES.

SACCHARIN STIMULATES BODILY OXIDATION.—That saccharin is harmless, and at the same time worthless as a provider of energy is now generally admitted. Its influence on the process of oxidation

has not been previously investigated. The author and Neill have previously shown that sugar, when ingested with other foods, stimulates the secretion of catalase, and hence increases the process of oxidation in the body. It is now found that saccharin has a much greater action in this direction than sugar. In this respect saccharin is, therefore, a positively helpful adjunct to the dietary. It is specially valuable in a disease such as diabetes, where the principal trouble is defective oxidation. (W. E. Burgo, *Science*; *J. Soc. Chem. Md.*, 38: 7, R, 1919; through *The Pharm. Jour. and Pharmacist*, October 11, 1919.)

CHLOROPICRIN VAPOR TO KILL BED BUGS.—Chloropicrin, when used in the proportion of 4 to 10 Gms. to each cubic meter of the capacity of the chamber treated, is an excellent means for destroying bugs. The method has been used successfully in ridding military beds of these insects. Four hours after vaporizing a small, closed chamber containing the beds, all the insects were dead. During the process of vaporizing a military gas mask is a perfect protection to the operator. In case eggs are not destroyed by the first treatment, a second fumigation should be performed at an interval of eight days. (G. Bertrand, Brocq-Rousseau and Dassonville, *Compt. rend.*, 169: 441, 1919; through *The Pharm. Jour. and Pharmacist*, October 11, 1919.)

KEROSENE AS A REMEDY FOR HARVEST BUGS.—Immediate relief is stated to follow the application of kerosene to the so-called "bites" of the harvest bug, or mowers' mite (*Leptus autumnalis*). In California, the mite is very prevalent among hay. The intense itching caused by the "insects" burrowing beneath the skin is often sufficient to incapacitate the victim from work. The intense irritation causes loss of sleep, and lesions are produced by scratching. All published remedies have proved useless, but the application of kerosene to the body before commencing work in the fields, changing the clothes when the day's work is over, and at once applying a little kerosene to any irritating spots as soon as observed, have given excellent results in alleviating the discomfort caused by this familiar seasonal pest. (Nona Allen, *J. Amer. Med. Assoc.*, 73: 628, 1919; through *The Pharm. Jour. and Pharmacist*, October 11, 1919.)

SUBSTITUTE FOR CACAO IN SUPPOSITORY BASIS.—As a substitute

for oil of theobroma, and to economize the use of spermaceti, which is now difficult to obtain, a mixture of one part of that substance melted in three parts by weight of olive oil may be used. This basis melts at  $37.2^{\circ}$  C. It is stated to be quite satisfactory for suppositories made by the warm method, but is not applicable for those made by pressure by the cold method. (*Pharm. Post.*, 51: 562, 1918; *Chem. Abstr.*, *Amer. Chem. Soc.*, 13: 1041, 1919.)

EXTRACT OF GLYCYRRHIZA.—For her thesis at Montpelier, Miss G. Pichard undertook a study of the different methods of preparing extract of licorice. The extracts prepared by the use of warm water possess a bitter taste, due to the content of resin present in the bark (10–14 per cent.), which is almost insoluble in cold water. In addition, the glycyrrhizin undergoes partial hydrolysis, so that this method should be rejected. She comes to the conclusion that the method of the U. S. P. gives the highest yield of glycyrrhizin percolation with the addition of solution of ammonia producing a content of 8 per cent. of this glucoside, compared with 4.5 per cent. obtained by percolating with cold water only. (From *The Chemist and Druggist*, October 4, 1919.)

BENZYL BENZOATE IN PROTOZOAL DYSENTERY.—The authors have employed benzyl benzoate in the treatment of eight cases of endamebic dysentery uncomplicated by bacillary infection, and have seen markedly good results in every case. All the cases were of the acute type and varied in severity. No ill effects on the alimentary or excretory tracts followed the administration of benzyl benzoate. In no case has the drug unfavorably altered the course of any case. On the contrary, its administration has always been accompanied by a marked alleviation of both the objective and subjective symptoms of the disease. It gives the patient much needed rest and permits him to sleep at night. Under the administration of the drug the endamebas disappeared from the stools in nearly every case as the general symptoms subsided. The benzyl benzoate we administered in a small amount of cold water, three times a day, after meals. The doses employed varied from 20 to 30 drops of the 20 per cent. alcoholic solution. (From *Jour. Amer. Med. Assoc.*, Oct. 25, 1919.)

*Significance of Small Amount of Sugar in Urine.*—If with hyper-



tension and chronic nephritis there is but an occasional trace of sugar in the urine and the blood sugar is not unduly high, then, Hamman says, the disordered carbohydrate metabolism must be subordinated to the renal or vascular condition. If there is marked glycosuria and the blood sugar is unusually high, then the diabetes must be emphasized. The clinical history is of importance. Patients past middle life with mild diabetes often gradually develop nephritis and hypertension, so that finally the renal and vascular conditions assume the prominent position in the clinical picture. On the other hand, Hamman has observed patients with hypertension over a number of years and has seen them gradually develop glycosuria and finally a definite intolerance for carbohydrates. (*Canadian Med. Assoc. Jour.*; through *Jour. Amer. Med. Assoc.*, December 6, 1919.)

*Use of Platinum Chlorid in Pneumonia.*—Anklesaria has made use of a 0.1 per cent. solution of platinum chlorid in 5 minim doses, in combination with Burney Yeo's effervescent quinine mixture, every four to six hours, in the treatment of pneumonia. He claims to have had very good results. The effect in some instances was really very striking. Within twelve hours of the treatment a noticeable change for the better was observed. He has also used quinine in a somewhat different form and manner. An ounce of good quinine is well rubbed with an equal quantity of powdered carbonate of ammonia. The powder is then made into a paste with an ounce of liquor ammoniae and set aside for an hour. Absolute alcohol, 4 ounces, is now added to the paste and the solution is filtered. The filtrate thus obtained is added to a pound of aromatic spirits of ammonia (B.P.). The clear mixture is labeled mixture of quinine carbonate, 1 : 20. It is prescribed as follows:

	Gm. or Cc.	
R̄ Sodii bicarbonatis.....	4	3 j
Mist. quininea carbonatis.....	8	3 ij
Vini ipecacuanhae.....	2	3 ss
Syrup aurantii.....	24	3 vj
Aquae anisi.....q. s. ad....	180	3 vj
M Ft. misturam.		
Sig. One ounce every four to six hours.		

To the mixture for an adult, 10 minims of a 1 : 1,000 platinum chlorid solution are added on the first day, 7.5 minims on the second

day, 5 minims on the third day, also on the fourth day if necessary, and then it is continued in 3 or 5 minim doses until recovery. (*Indian Med. Gaz.*; through *Jour. Amer. Med. Assoc.*, December 6, 1919.)

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## CORRESPONDENCE.

THE UNIVERSITY OF WISCONSIN,

MADISON.

Editor, AMERICAN JOURNAL OF PHARMACY,  
Philadelphia, Pa.

In order to be able to assist one of our students, majoring in art, who is making a special study of pharmaceutical book plates, I take the liberty to ask all persons or associations that have book plates to send specimen copies. Your kind coöperation in publishing this notice, as well as theirs will be greatly appreciated. If librarians and other book lovers who know of such book plates, old as well as new, will kindly advise the writer of their discoveries, it should be possible to make the catalogue of pharmaceutical *ex libris* much more complete than would otherwise be the case. Trusting that this appeal may meet with many a response, I remain

Very truly yours,

EDWARD KREMERS.

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## BOOK REVIEWS.

SOLUBILITIES OF INORGANIC AND ORGANIC COMPOUNDS. By Ather-ton Seidell, Ph.D., Hygienic Laboratory, U. S. Public Health Service, Washington, D. C. Second edition, enlarged and revised. \$7.50 net. D. Van Nostrand Company, New York.

This is a compilation of quantitative solubility data from the periodical literature gleaned from fifty periodicals during the years 1900 to 1917 inclusive, twenty-three periodicals being searched page by page and the other twenty-seven through tables of contents, and represents the study of about 2600 different substances by more than 1500 investigators. The first edition came out in February, 1907, and a second printing with corrections appeared in

1911. In this edition there were 354 pages of subject matter and  $10\frac{1}{2}$  pages of index. The present edition (February, 1919) contains 784 pages of body matter, 37 pages of author index and 21 pages of subject index. Most of the body of the book is devoted to tabular arrangements of solubility data, but there are 18 pages of general information explaining the use of the tables and giving reasons for the appearance of some of the data in the book; and there are 28 pages on methods for determining solubilities, with illustrations of the most important of the apparatus described in the text.

The names of the substances for which solubilities are given are arranged alphabetically, the pages and paragraphs being headed in bold-faced type for easy reference. The authority for the data in each instance is given by name of author and year data was published, while in the back of the book are to be found two pages giving the names of the 50 periodicals from which the data were collected, pagged so that the original article can be traced easily.

In preparing a review of a book of this character it is difficult to find a place of attack, as the reading of 784 pages, chiefly of tabular matter in rather fine print, is apt to be exceedingly tiresome without "getting one anywhere." Something of the scope of the book may perhaps be gathered from the examination of the data given for a few substances. Taking seven somewhat at random, we find that:

For Quinine (p. 576) the solubility is given in 19 different liquids, in some at 3 different temperatures.

For Radium Emanations (p. 580) the solubility is given in 15 liquids, at  $0^{\circ}$  C. and at  $18^{\circ}$  C.

For Carbon Dioxide (p. 44) the solubility is given in 44 different liquids, at 3 different temperatures.

Five pages are devoted to solubilities of Phenol, eight to Ethyl Alcohol, ten to Mercuric Chloride, nine to Iodine, each in a great variety of liquids and under a great variety of conditions. In the case of Iodine (for illustration) the solvents named include water, alcohol, benzene, chloroform, ether, bromoform, carbon disulphide, carbon tetrachloride, aqueous solutions of potassium iodide, mercuric chloride, potassium bromide, sodium chloride, hydrochloric acid and a number of other salts and acids, together with a lot of mixed solvents, each substance being used in various strength solutions.

One who examines the subject matter of the book, even very superficially, cannot help being amazed at the vast amount of work

the determination of the facts recorded therein represents, on the part of the original workers or investigators; nor can he help being impressed with the vast amount of painstaking labor that must have been done by the author of the present volume in its compilation. In the preface the author says: "The principal object in preparing a compilation of solubility data, from the point of view of the advancement of chemistry, is to furnish material for the origination and verification of theories of solution," but one can readily see how this volume may be of great value to anyone whose work has to do with the solubility of substances in various solvents and under varying conditions.

F. P. STROUP.

ANNALS OF THE MISSOURI BOTANICAL GARDEN, Vol. 6, No. 3, Sept., 1919.

AN EDIBLE GARDEN *HEBELOMA*.—E. A. Burt describes and pictures an edible *Hebeloma*, which he found in great abundance in cultivated borders of the Missouri Botanical Garden on June 3rd, and which he names *H. hortense*.

This species differs from the majority of other members of the genus *Hebeloma* in that its fructifications are devoid of viscosity and odor of radishes and its occurrence in abundance in cultivated ground. Nearly all the other species of *Hebeloma* are found sparingly in forests and are either inedible or poisonous.

PROTOMERULIUS FARLOWII.—The same author describes and pictures another fungus which was collected by Dr. Farlow at Chocorua, New Hampshire. This he named "*Protomerulius Farlowii*." Its fructifications occur on rotten, decorticated, coniferous wood in small gregarious patches, each being gelatinous, membranous, very thin and tender, purple when fresh, becoming pale olive-gray on drying, showing under the microscope an imperfectly porose surface with thin, irregular folds and more or less lacerated dissepiments.

THE MICRO-CALORIMETER IN THE INDICATOR METHOD OF HYDROGEN ION DETERMINATION.—B. M. Daggar finds that the Duboscq type of micro-colorimeter lends itself admirably to determining the H ion concentration in small quantities of fluids. The procedure is briefly described and the method of standardizing the apparatus carefully explained.

STUDIES IN THE PHYSIOLOGY OF THE FUNGI. VIII. MIXED CULTURES. By S. M. Zeller and Henry Schmitz.—The authors discuss the behavior of the following fungi in mixed cultures: *Lenzites vialis*, *Merulius pinastri*, *Daedalea quercina*, *Trametes Peckii*, *Pleurotus sapidus*, *Merulius lacrymans*, *Lentinus lepideus*, *Daedalea confragosa*, *Coniophora cerebella*, *Polystictus versicolor*, *Isaria* sp., *Polyporus lucidus*, *Polystictus hirsutus*, *Aspergillus glaucus*, *A. niger*, *A. fumigatus*, *A. versicolor* and *A. Sydowi*. A number of combinations were used and the results indicated in two tables. A plate of 12 figures, illustrating the nature of combination growths in culture media accompanies the article.

STUDIES IN THE PHYSIOLOGY OF THE FUNGI. IX. ENZYME ACTION IN *Armillaria Mellea* Vahl, *Daedalea Confragosa* (Bolt. Fr., and *Polyporus Lucidus* (Leys.) Fr. By Henry Schmitz and Sanford M. Zeller.—In this article the authors discuss the enzyme activities of the fungi indicated. In *Polyporus lucidus* the presence of the following enzymes is demonstrated: Esterase, maltase, lactase, sucrase, raffinase, diastase, inulase, cellulase, hemicellulase, emulsin, tannase, urease, and trypsin and erepsin, when fibrin is used as a substrate.

In *Armillaria mellea* the presence of the following enzymes is shown: Maltase, lactase, sucrase, raffinase, diastase, inulase, cellulase, hemicellulase, emulsin, urease, amidase, and trypsin and erepsin, when fibrin is used as a substrate.

In *Daedalea confragosa* the following ferments are present: Esterase, maltase, lactase, sucrase, raffinase, diastase, inulase, cellulase, hemicellulase, emulsin, tannase, urease, and trypsin and erepsin, when fibrin is used as a substrate.

A new method for the determination of ammonia liberated by amidase is described.

STUDIES IN THE PHYSIOLOGY OF THE FUNGI. X. GERMINATION OF THE SPORES OF CERTAIN FUNGI IN RELATION TO HYDROGEN ION CONCENTRATION. By R. W. Webb.—The author reviews the literature bearing on this problem and then discusses the methods he followed in determining the effect of hydrogen ion concentration upon the rate of germination of the spores of certain fungi and the range within which most favorable germination occurs. He draws the following conclusions:

(1) In a culture solution consisting of M/5 mannite, phosphoric

acid, and sodium hydroxide, successively increasing concentrations of hydrogen ions from neutral or approximately neutral to PH. 3.1-2.8 favorably influence germination of the spores of *Aspergillus niger*, *Penicillium cyclopium*, *Botrytis cinerea*, *Fusarium* sp., and *Lenzites saepiaria*.

(2) The range of germination and the magnitude of the germination quantities as influenced by hydrogen ion concentration in the solution depend upon the organism, germination being obtained with the following concentrations, inclusive: *Aspergillus niger*, PH. 2.8-8.8; *Penicillium cyclopium*, 2.9-10.0+; *Botrytis cinerea*, 2.8-7.0; *Fusarium* sp., 2.8-10.0+; and *Lenzites saepiaria*, 2.8-7.0.

(3) It is not until a hydrogen ion concentration of PH. 2.8 or above is reached that inhibition of germination of the forms studied is noticed.

(4) *Aspergillus niger*, *Penicillium cyclopium*, *Botrytis cinerea* and *Lenzites saepiaria* show a maximum of germination in the medium employed at PH. 2.8-3.1; *Fusarium* sp. exhibit a secondary maximum at this concentration.

(5) *Fusarium* sp. give a pronounced maximum of germination at PH. 7.4 and *Penicillium cyclopium* exhibit a minor secondary maximum at PH. 7.0-7.4.

(6) For equal removes from the neutral point, OH ions appear to be relatively more toxic to the spores studied than H ions.

(7) With increase in length of intervals of incubation, the relations of germination to hydrogen ion concentration remain practically the same.

(8) The curves of germination for any organism are practically identical, whether incubated at 22° C., 27° C., or 31° C.

HEBER W. YOUNGKEN.

A CRITICAL REVISION OF THE GENUS EUCALYPTUS. By J. H. Maiden, I.S.O., F.R.S., F.I.S. Vol. IV, Part 8.

The part of this comprehensive monograph on the Genus *Eucalyptus* that is now before us continues this work along the lines of the preceding parts. The same high-class illustrations are likewise continued. It presents descriptions of the following species:

*Eucalyptus tessellaris* F.v.M; *E. Spenceriana* Maiden; *E. Cliftoniana* W. V. Fitzgerald; *E. setosa* Schauer; *E. ferruginea* Schauer;

*E. Moorei* Maiden and Cambage; *E. dumosa* A. Cunn; *E. torquata* Luehmann; *E. amygdalina* Labill; *E. radiata* Sieber; *E. numerosa* Maiden; *E. nitida* Hook. f.

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#### BULLETINS OF THE UNIVERSITY OF WISCONSIN.

It is a pleasure to review the two bulletins of the University of Wisconsin that have recently come to hand.

The first of these bulletins is a study of the Galenical Oleoresins, by Andrew G. Du Mez, and is a thesis submitted for the degree of Doctor of Philosophy at the University of Wisconsin. The history and bibliography of this class of preparations has been very carefully compiled. A review of the work done by various investigators on each of the official oleoresins is thus brought together and compared in the various tables. In addition to the bibliographic study involved by this comprehensive review of the subject covering 288 pages, there is considerable original investigations of the various methods proposed for the manufacture of oleoresins and the chemistry of the individual preparations. It exhibits a high type of study and research work and demonstrates that the research spirit in pharmacy in America is not inactive. Furthermore, that the Department of Pharmacy of the University of Wisconsin and several more of the schools of pharmacy are stimulating the research spirit by requiring thesis contributions for degrees in course. This is an example which might well be followed at least by all schools claiming to educate in the higher courses in pharmacy.

It is regretted that the space at our command will not permit of the reprinting of abstracts of this valuable thesis which should be read by all interested in the development of pharmacy and its literature and preserved as a work of reference on this subject.

The second of these bulletins is a thesis by Nellie A. Wakeman, likewise submitted for a degree at the University of Wisconsin. It is upon the subject of "Pigments of Flowering Plants." The subject of pigmentation in plants is one that is of especial interest to both chemists and botanists. The author of this thesis, under the guidance of Prof. Edward Kremers, has also performed a valuable service in presenting this comprehensive bibliographic study of such an interesting subject. Numerous structural and graphic formulas are given, illustrating the chemical composition of the various organic com-

pounds producing the colors in vegetation. It likewise is a most commendable and valuable contribution to our literature.

G. M. B.



# THE AMERICAN JOURNAL OF PHARMACY

FEBRUARY, 1920

## EDITORIAL.

### THE PROHIBITION ENACTMENT AND THE TREASURY REGULATIONS FOR ITS ENFORCEMENT.

The pamphlet "Regulations 60" of the Bureau of Internal Revenue, has been issued to cover the manufacture, sale, barter, transportation, importation, delivery, furnishing, purchase, possession, and use of intoxicating liquor under Title II of the National Prohibition Act of October 28, 1919, commonly spoken of as the Volstead Act. The purpose of this Title of the law is to provide for the enforcement of the Eighteenth Amendment of the Constitution of the United States, and the regulations now promulgated by the Federal Prohibition Commissioner are issued by virtue of the authority conferred upon the Commissioner of Internal Revenue by that Act.

Those engaged in the drug business, either as pharmaceutical manufacturers, as wholesale or retail druggists, or as dispensing pharmacists, must again apply themselves to the studying of another series of regulations. In the recent years, it would seem that the series of Departmental regulations and of supplements, amendments and rulings have followed so closely that a large portion of their time has been consumed in becoming acquainted with the requirements so as to comply therewith and avoid unintentional violation.

Physician and pharmacist alike will be compelled to unlearn some of the procedures which but recently they were compelled to follow in compliance with prior regulations, as the present issue of decrees materially changes a number of the former promulgations. This will become a matter for further confusion and considerable annoyance. We are brought to realize that the laws of our country are not like those of the Medes and Persians, and we must regret that there is not likewise more stability shown in Departmental regulations.

In the prior regulations, the pharmacist was given a choice of ten formulas for the medication of alcohol for sale for bathing purposes or as antiseptics without prescription, in quantities of less than one pint. Under the new regulations, he becomes restricted to the use of seven formulas. The two most commonly used formulas (carbolic acid 1 part, alcohol 99 parts; and formaldehyde 1 part, alcohol 250 parts) with which physicians and patients had become acquainted are now omitted from such permissible formulas. He must now repeatedly explain why acts and sales heretofore made and complying with official orders are now forbidden by edict from the same department. Formerly, he was forbidden the privilege of preparing such medicated alcohol in advance of order and then only in the restricted amount of purchase limited to one pint, now the wholesale druggists may so medicate alcohol and sell this in any amount to holders of permits to purchase, including retail druggists, pharmacists, Turkish bath establishments, and any person desiring to procure such medicated alcohol for legitimate external use may obtain a special permit to obtain same in any quantity desired.

T. D. 2788 denied the pharmacist the right to sell distilled spirits and wines for internal use as *medicine even on a physician's prescription*. T. D. 2881, issued a few months later, provided that "physicians may prescribe wines and liquors for internal use, or alcohol for external use, but in every such case each prescription shall be in duplicate, and both copies be signed in the physician's handwriting. The quantity prescribed for a single patient at a given time shall not exceed 1 quart," and declared "all prescriptions shall indicate clearly the address of the patient, the date, the condition or illness of the patient and the name of the pharmacist to whom the prescription is to be presented for filling." According to the present rulings, and the law, the physician who has a permit to prescribe liquors may prescribe for a patient under his care not more than *one pint* of spiritous liquor to be taken internally within any period of ten days and he need not state on the prescription the condition or ailment for which the liquor is prescribed nor the name of a pharmacist who is to dispense the prescription. It is thus seen that in less than one year's time there have been three different regulations promulgated as to prescriptions, and it is not at all strange that the busy physician and pharmacist should be confused by these frequent changes.

The official form on which the prescriptions for liquors must hereafter be written assign so much space for the data

required that scarcely sufficient space remains for the prescription proper and the directions and the physician will be compelled to write in a small handwriting or to abbreviate in order to get this necessary matter within the space allotted therefor. The book of records required of the physician must show the date of issue of each prescription, amount prescribed, for whom and the purpose or ailment for which it is to be used and the directions stating the frequency and the dose. The official record book that is being supplied to physicians for such records has on the initial page the printed rules and regulations and a sample of the record that is expected. This type prescription directs as a dose for the 8 ounces of whiskey directed, "a wineglassful." It is not presumed that this was intended by the prohibition officer as advisory for an average medicinal dose and yet the matter is too serious to suspect a pun on the needs of sick mortals.

The drug trade and other manufacturers whose business compels the use of pure alcohol or other distilled or vinous spirits were given assurance that the regulations that would be framed under this act would be reasonable and bear in mind the needs of medicine and that no unnecessary restraint or hindrance would be placed in the way of these industries or professional practices. The regulations as promulgated are disappointing in many respects and would appear as if a studied attempt had been made to drop wherever possible a monkey-wrench into the machinery of the medical practice and the industries associated with the drug trade.

The manufacture of medicines must be considered as preëminently a "lawful industry" and the title of this Act states that one of the purposes that Congress had in mind was "to insure an ample supply of alcohol" and "to promote its use in scientific research and in the development of lawful industries." It would seem that the officials in the framing of the regulations had in mind the surrounding of the procuring of alcohol for such essential industries with as much red tape as possible and to impede rather than facilitate their manufacture and to promote industrial development. As the Department has absolute control of the granting of permits to buy and use such liquors and each purchase can only be made subject to the approval of the application to withdraw, and the permit may be revoked and severe penalties imposed for misapplying the alcohol so withdrawn it would seem that the officers of this bureau have ample means of

protecting against fraud and the punishment of violations without the need for unnecessary exhibitions of bureaucratic authority.

Congress in each of its conservation and prohibition enactments and likewise in the wording of the Eighteenth Amendment, recognized the need for distilled spirits and wines for medicinal purposes and exempted such and made special provisions for a less tax thereon as being used for non-beverage purpose. It is inconceivable that, in the light of such action and in this enlightened country, restrictions such as this law and the regulations provide should hamper the legitimate practices of medicine and pharmacy.

The procuring of the necessary supplies of alcohol by the pharmacist must at times prove a hardship and may even imperil the lives of many people. Before his order for this essential ingredient in many of his preparations can be filled, he must make application in triplicate and an additional copy must be made of the application for each carrier through whose hands the shipment must pass and after he has made affidavit thereto and obtained the approval of the prohibition director of his district he may send these with his order to the vendor. If the pharmacist is situated in the same city as the prohibition district officer or in a nearby city such a procedure may not entail any great delay. If, however, his business is located in a community some distance away from the office of the district prohibition officer, several days may elapse before his application can be honored and reach the source of his supply. In the event of an epidemic, such as the recent experiences with influenza, he may find his stock of necessary medicines exhausted and the immediate renewal impossible because of the delay in securing supplies of alcohol.

As we have studied the recent laws and the regulations of the Federal Departments we have been compelled at times, against our will, to criticise the lack of knowledge of fundamental facts and the inconsistencies and incongruities that have been incorporated therein. The Volstead Act and "Regulations 60" are no exceptions and contain much that is false, inconsistent and subject to criticism.

A great need of the time is that Congress in the framing of enactments should accept the advice of reliable, experienced manufacturers, business men and the professions concerned in the legislation rather than the baseless opinion and guidance of fanatics and radicals and their hired propagandists. Many recent enactments and departmental regulations contain statements that are not in accord

with established scientific facts or common sense and some that border on the ridiculous and that such should appear in the statutes of the Federal Government is certainly not creditable to the American law makers. These but accentuate the need for a broader-minded statesmanship that will solicit the advice of those whose experience, ability and actual knowledge qualifies them as safe advisers. The tendency has been to pass acts of Congress that the proponents have not even been able to explain and to leave entirely too much to the "regulations to be framed" by a department or an official. As a result there has developed a marked trend toward interpreting the law and interpolating sentences and clauses therein by the departments and the regulations are in some cases viewed as the law to the exclusion of the intent of Congress. It is time that Congress found itself again and assumed its prerogative as the law-making body and framed its acts in language that is clear and accurate and leaves no doubt that the sole duty of a department is the enforcement of the provisions in accordance with the law's intent.

No sound explanation has as yet been given as to the meaning of the words "unfit for use for beverage purposes" as used in this Act in connection with medicinal preparations of the U. S. P. and N. F. or the Homeopathic Pharmacopoeia, or to medicines, toilet, medicinal and antiseptic solutions and flavoring extracts. The attempt of the regulations to interpolate does not clarify the wording of the act. The development of the art of pharmacy has been to make pharmaceutical preparations pleasant and their efficacy quite often is traced to palatability that makes the medicine so inviting that it will be taken regularly and retained. This has been the trend of modern medicine and it is inexplicable that Congress should have been ignorant of this or that it aimed to destroy rather than "promote the development" of medicine and pharmacy. The purpose of the law is evidently to exempt the use of alcoholic liquors as medicines or when used in the preparation of medicines so as to comply with the provisions of the Amendment.

The Commissioner has exercised the authority vested by declaring in the regulations that eighteen of the preparations of the U. S. P. and N. F. are held to be fit for beverage purposes. Further, that while distilled spirits and wines may be used in their manufacture these preparations may not be used or disposed of except in the manufacture of other preparations or medicines which are unfit

for beverage purposes. The list consists mainly of vehicles for the administration of disagreeable medicines, and the fact that their inclusion in the Pharmacopoeia or Formulary is proof of such general use in medicine throughout the country that it was necessary to establish standard formulas, makes no impression upon the attitude of the commissioner. By further injudicious extension of authority this list might be extended many fold by the inclusion of other titles. It would appear to the layman that the plain duty of the enforcement officers was to punish every violation of the use of these as medicines and not to take a course that will detract from their proper use as medicines.

In the promulgation that tartar emetic must be used as a denaturant for bay rum the commissioner has declared what we believe is a dangerous precedent. To insist that such a toxic substance as a soluble salt of the poisonous metal antimony shall be added to bay rum that is extensively used for bathing infants and invalids and as a vehicle for applications to the scalp and skin is laying a multitude of death traps and it will be fortunate indeed if serious accidents do not occur through this action. We urge that physicians and especially dermatologists be advised of this medication so that they may select some other vehicle in place of *antimoniated bay rum*. A thorough scientific investigation should have been made to determine the effect of tartar emetic upon the skin, hair and organs of the body. The chemical analogy existing between antimony and arsenic is so close that similar chronic poisonous effects and depilatory action may be anticipated.

The Departments of the Federal Government are not working in harmony. The Bureau of Chemistry is rightly prosecuting for adulterations manufacturers whose medicinal preparations deviate from the standards laid down in the U. S. P. and N. F. and the most vicious form of adulteration is the addition of a poisonous or deleterious substance. The U. S. P. and N. F. fix the legal standards for alcohol and for compound spirit of myrcia and if these are sold as medicines "for internal or external use" they are classified under the Federal Food and Drugs Act as drugs and must comply with the "standard of strength, quality or purity as determined by the test laid down in the United States Pharmacopoeia or National Formulary official at the time of investigation." The Pharmacopoeia lays down a standard for alcohol and all alcohol sold for use as a "drug" must comply with that standard. The National Formulary lays

down a standard for compound spirit of myrcia and all compound spirit of myrcia sold as a "drug" must comply with that standard. The law does not recognize as the standards of *strength, quality and purity* the U. S. P. or N. F. products plus the addition of bichloride of mercury, formaldehyde, tartar emetic or other poisonous or deleterious substances, and the additions to alcohol and bay rum directed in the regulations unquestionably are adulterations as they cause deviations in strength, quality and purity from the legal standards. The Bureau of Internal Revenue is thus advising and insisting that there must be a very general violation of the spirit and purpose of the Food and Drugs Act. It would appear to an observing mind that this was establishing a rather dangerous precedent, especially considering the deleterious nature of the additions named.

The law limits the dispensing of spirits and wines to the licensed pharmacist and on prescription only. This indicates that Congress considered this as part of the professional duty of pharmacists and not as acts of dealers in intoxicating beverages. Nevertheless, the regulations again require that pharmacists filling prescriptions for intoxicating liquors must pay the special tax as liquor dealers and keep the special retail liquor dealer tax stamp conspicuously posted. A new feature of the regulations is that pharmacists shall keep a record on a specified form of all intoxicating liquor received and disposed and make monthly reports of all such transactions.

The pharmacists will probably have considerable trouble in getting the physicians to understand the provisions relating to the method of writing the prescriptions and keeping the records required and the limitations to the quantity and uses of such distilled spirits. The physician is prohibited from prescribing liquor for his personal use and the pharmacist must refuse to fill such prescription if presented. Physicians must file application and obtain permit to prescribe. The prescription must be written on the official form supplied in book form by the Commissioner and contain all the data required and he must keep a copy thereof on the stub and the records in book form in the official record book supplied. He is limited to prescribing for persons upon whom he is in attendance and after careful physical examination of such person. Not more than one pint of spiritous liquor may be prescribed for the same person within any period of ten days. The liquor so procured may only be used for medicinal purposes by the person for whom prescribed. The pre-

scription can be filled but once and must be indorsed by the pharmacist "as cancelled" upon being filled and filed on a special file.

Physicians are permitted to purchase on permit without bond not more than six quarts of liquor during any calendar year *to be administered to their patients only* in quantities necessary to afford relief at the time of administering and may not sell or furnish the same to such person or to any other persons.

A special regulation permits physicians of the homeopathic and eclectic schools to secure on a blanket form good for 90 days, supplies of alcohol and potencies and dilutions and such physicians can receive without bond not in excess of 15 gallons of alcoholic preparations during any one calendar year. The reason for such special regulation and discrimination in favor of the dispensing physicians of these schools is not clear. Under the prior regulations all dispensing physicians of any school were required not only to obtain permits but likewise to give bonds with the exception that not exceeding 2 drachms of any attenuation, potency or dilution could be purchased at a time by anyone without filing bond or obtaining a permit. It is hard to reconcile as consistent promulgations from the same bureau within one year regulations that fix such a wide variation in limits to do the same act legally as 2 drachms and 15 gallons. An expansion of 7,680 times in so short a space of time is indeed hard to explain on rational grounds. G. M. B.

#### OFFICERS-ELECT OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

The Board of Canvassers met in Chicago on January 21, to canvass the ballots received in the election by mail. Their report shows the following officers elected for the year 1920-1921:

President, Charles Herbert Packard, Boston, Mass.

First Vice-President, E. Fullerton Cook, Philadelphia, Pa.

Second Vice-President, Charles E. Caspari, St. Louis, Mo.

Third Vice-President, W. P. Porterfield, Fargo, N. D.

Members of the Council to serve for three years: Harry B. Mason, Detroit, Mich.; Lucius E. Sayre, Lawrence, Kan.; Frederick J. Wulling, Minneapolis, Minn.

Mr. Charles Herbert Packard, the president-elect, is a practical pharmacist owning two stores in the city of Boston. He was born in Amherst, Mass., 1863. His education was received in the public



schools of Boston and at the Arms Academy. He entered upon his pharmaceutical career in 1880 and was graduated from the Massachusetts College of Pharmacy in 1892. He has taken a very active interest in the affairs of his alma mater and has been a trustee of the college since 1904 and its president since 1909.

Mr. Packard is an indefatigable worker in all of his association connections and with energy and marked ability has filled many positions of honor and responsibility. He was the first president of the New England Branch of the A. Ph. A. and filled this position for three years. He has been a member of the Boston Retail Druggists' Association since that association was organized and has continuously held the office of treasurer thereof.

He was elected president of the Massachusetts Pharmaceutical Association in 1907. He has been a faithful attendant at the meetings of the American Pharmaceutical Association. In 1911 he was the local secretary at the Boston meeting and served as third vice-president in 1912 and second vice-president in 1914 and in 1913 was chairman of the general committee on membership and organized a campaign for membership.

He has been active in Masonic circles and also in other fraternal organizations and has been prominent as one of the progressive citizens and business men of his city, taking an active interest in civic affairs.

#### MEETING OF THE A. PH. A. EXECUTIVE COMMITTEE.

The first meeting of the Executive Committee of the Council of the American Pharmaceutical Association was held at the Planters Hotel in St. Louis, the opening session being scheduled for 10 A.M. Saturday, January 31. Those present were Lewis C. Hopp, President L. E. Sayre, Dr. J. H. Beal, Dr. H. M. Whelpley, Secretary Joseph W. England, William B. Day, George M. Beringer and some of the sessions were attended by Prof. Charles H. LaWall and F. W. Meissner, Jr., who had been in attendance at the meeting of the Board of Trustees of the U. S. P. at the same hotel, that had just adjourned.

The Committee held almost continuous sessions for two days and gave careful consideration to the numerous questions that had been referred to them. It is believed that the wisdom of this innovation in the procedure of the American Pharmaceutical Associa-

tion, by which questions of importance can be referred to a committee selected because of their experience, breadth of view and keen interest in the welfare of pharmacy, was demonstrated. The various problems presented were discussed in this round-table conference with intense interest and viewed from many angles and without the disturbing interferences that usually occur at the annual conventions or large gatherings. It was apparent that preconceived ideas gave way to logical conclusions arrived at by careful deliberation to determine what were to the best interests of the Association and to the advancement of pharmacy.

The much discussed subject as to the financial problems of the Association and the changes proposed in its several publications and activities having been referred to this committee was considered very carefully and every phase of the arguments was given due consideration. The committee concluded that the American Pharmaceutical Association could not curtail its activities in the least, that its services in behalf of the progress of pharmacy called for extension rather than contraction in any way. On the other hand it was very apparent that the cost of publication and the management of the work of the Association had very materially increased and that there was no likelihood of any early decline and retrenchment. No industry could expect to continue successfully for any length of time under pre-war prices and conditions. The A. Ph. A. has continued for upwards of fifty years, continually extending its service in the interest of pharmacy, without any advance of cost to its membership. The existing conditions required that each member should bear his just proportion of the necessary increased cost of management and the consensus of opinion was that the membership would cheerfully accept the recommendation of the committee that commencing with 1921 the dues of the Association should be made \$7.50, and that there should be no curtailment in the efforts and services rendered by the A. Ph. A. Parenthetically, it might be said, that the ideas advanced by the committee at this conference, if adopted, will materially broaden the scope of its activities. Unless the signs fail, pharmaceutical and drug trade circles will in the future hear much more of these suggestions.

The several propositions for minor changes in the *Journal of the A. Ph. A.* were taken up and it was found that some of these had already been adopted and others were in process for acceptance with such modifications as had to be made. The Committee on

Publication welcomed constructive criticism that will improve in any way the publications of the Association.

The subject of paramount importance considered by the executive committee was the creation of a nation-wide movement for pharmaceutical research. This movement is destined to be a potent factor in the development of the professional aspect of pharmacy and likewise of incalculable value to the public welfare.

The committee appreciated that much has already been accomplished by the studies of individual pharmacists and the efforts of the faculties of some of the schools of pharmacy. The numerous contributions thus made to our knowledge of remedial agents but open to view the ever-widening field awaiting pharmaceutical research. Our knowledge of but very few of the drugs that are in extensive use and daily prescribed can be said to be complete. The advances in medicine, chemistry and the collateral sciences are adding constantly new materials to the innumerable drugs and chemical substances that are used as remedial agents and require thorough investigation from the viewpoint of pharmacy.

The systematic investigation of the processes of pharmacy, the sources and methods of preparation of many drugs, their composition and the valuable therapeutic and economic constituents, their extraction, estimation, standardization and their therapeutic application are some of the avenues open to pure pharmaceutical research or to investigations in collaboration with collateral research. The need is that this broad field open to pharmaceutical research should be exploited not by individual or by sporadic efforts of committees too often lacking in both the necessary moral and financial support but by a comprehensive development carefully planned and systematically carried on.

The various endowments for research already created or in contemplation have given little or no consideration to the needs of pharmacy and the importance and possibilities of the benefits that would accrue to the world's welfare and progress from systematic scientific investigations in the field that is peculiar to pharmacy. There is open to pharmacy a vast domain for research that is separate and distinct from the specialized fields occupied by the established research endowments. The various pharmaceutical and drug trade organizations have long recognized this and through the medium of various committees have individually aimed, to the ex-

tent of their ability, to stimulate and promote pharmaceutic research and many valuable contributions have resulted from their efforts.

The executive committee are convinced that the time is fully ripe for the crystallization of the sentiment favoring a distinct pharmaceutical research and the combination of the various interests that have been working in that direction into a united movement and concerted action to bring this about. They propose that the American Pharmaceutical Association shall take the initiative and propose the establishment of THE AMERICAN PHARMACEUTICAL RESEARCH ENDOWMENT. The purpose of which shall be to promulgate, systematize and coördinate scientific investigations in the special fields open to pharmacy so that investigators may be stimulated and scientific studies carried on in the most effective manner in order that the greatest volume of accurate knowledge may be collated and the greatest benefit accrue to mankind.

The plan proposed is that all of the national pharmaceutical, drug and chemical organizations shall be invited to join in the foundation of the Research Endowment; that the management and control of the funds and the research shall be under the direction of a Board of Trustees to be composed of one representative selected by each of the organizations joining in the incorporation and foundation of the endowment. Contributions, donations and bequests to this endowment are to be solicited from corporations, firms and individuals. These shall have the privilege of endowing special professorial chairs, fellowships or to make contributions to be applied toward any particular line of investigation desired. The trustees shall have power to invest and reinvest the funds and securities of the endowment, to select a director of research and to organize a staff of assistants, students and investigators, to make grants and awards, to acquire by rent, purchase or acceptance, suitable offices, buildings and grounds and the equipment needed; to organize such a force of clerks and assistants as may be necessary and to perform all acts required for the carrying into effect the work and plans of the endowment.

The broad view taken and the comprehensive plan thus outlined is presented to the pharmacists of America and to the public who are to reap the greatest good therefrom with the expectation that it will receive careful and critical consideration. It is a basic plan on which the various drug trade organizations and scientific bodies of

pharmacy should be able to effect a permanent, strong and well-rounded-out plan for the systematic development of scientific research along lines that are very properly claimed as the distinct field for the investigations of scientific pharmacy. The fact that while it is to be advocated by the American Pharmaceutical Association no one organization will have a predominating voice in the management but that each association or interest joining in the foundation will have an equal share in the responsibility of management and in the working out of the details of the plan, is a strong point in its favor as it is at once removed to the high plane of a truly altruistic movement that should merit endorsement and the hearty support of all.

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## IONIC DISSOCIATION AND HYDROGEN-ION CONCENTRATION.

BY FREEMAN P. STROUP, Ph.M.,

PHILADELPHIA, PA.

Aristotle is credited with having once said, "Nothing can be positively known and even this cannot be positively asserted." The chemist who reviews the various theories that have been advanced to explain chemical composition and chemical reactions is inclined to believe the old philosopher was right, at least in so far as the statement applies to things chemical. If we could see the ultimate particles which make up what we call matter, and could study their movements, we could be more positive in our conceptions. Man is a theorizing animal, and that which he cannot see he tries to explain by imagining things about it. Such has been the history of chemical theory.

The greater the number of facts that can be consistently explained by one and the same theory the greater the probability of its being true. The Ionic Theory consistently explains so many things which, before its promulgation by Arrhenius, were inexplicable by any of the theories previously held that, though there are yet some known facts which do not seem to be in accord with it, chemists generally accept it as being the true one. It is not my intention at this time to go into a discussion of the facts that either demonstrate its truth or

tend to discredit it, as these are taken up with more or less detail by most of the textbooks on general chemistry which have been published or thoroughly revised during the last ten or fifteen years.

As we study chemical compounds we find that some, when dissolved in certain liquids (water, in particular), conduct the electric current in proportion to the concentration of the solution, while others do not. To the class of substances which conduct the current, hence called "electrolytes," belong the three great classes of compounds—acids, bases and salts.

According to the Ionic Theory, electrolytes, when dissolved in a so-called "dissociating solvent," decompose wholly or in part—dependent upon the nature of the substance and the concentration of the solution—into two sets of particles or molecules, the members of one set being charged with positive electricity, the members of the other set being negatively charged, and the number of positive charges just balancing the number of negative charges, the solution being electrically neutral. These charged particles are called "ions" (meaning wanderers), those of positive charge being known as "cations," those of negative charge, "anions." When an electric current is caused to pass through such a solution the cations move toward the negative electrode (the "cathode") and the anions move toward the positive electrode (the "anode") of the decomposing cell, there losing their charges and either separating as elements or forming new combinations with the water of the solution or with some substance in the solution. Electrolytes are frequently called "ionogens."

*Acids* may be defined ionically as compounds which, when dissolved in a dissociating solvent, such as water, yield hydrogen ions, frequently called "hydrions."

Examples:  $\text{HCl} = \text{H}^+ + \text{Cl}^-$ ;  $\text{HNO}_3 = \text{H}^+ + \text{NO}_3^-$ ;  $\text{H}_2\text{SO}_4 = \text{H}^+ + \text{H}^+ + \text{SO}_4^{--}$ .

The hydrions are the cations, the  $\text{Cl}$ ,  $\text{NO}_3$ ,  $\text{SO}_4$ , etc., are the anions, sometimes called "acid ions" to correspond with the old designation "acid radicals," as well as to make the matter more easily understood by persons familiar with the older theories.

*Bases* may be defined ionically as compounds which, when dissolved in a dissociating solvent, yield hydroxyl ( $\text{OH}$ ) ions, also known as "hydroxidions."

Examples:  $\text{KOH} = \text{K}^+ + \text{OH}^-$ ;  $\text{Ca}(\text{OH})_2 = \text{Ca}^{++} + \text{OH}^- + \text{OH}^-$ ;  $\text{NH}_4\text{OH} = \text{NH}_4^+ + \text{OH}^-$ .

The hydroxidions are the anions, while the K, Ca,  $\text{NH}_4$ , etc., are the cations, sometimes called "metal ions," for reasons similar to those given under acids.

*Salts* may be defined ionically as compounds which, when dissolved in dissociating solvents, yield cations other than hydron and anions other than hydroxidion. The cations of salts are the cations of bases and the anions are those of the acids.

Examples:  $\text{NaCl} = \text{Na}^+ + \text{Cl}^-$ ;  $\text{Ca}(\text{NO}_3)_2 = \text{Ca}^{++} + \text{NO}_3^- + \text{NO}_3^-$ ;  $(\text{NH}_4)_2\text{SO}_4 = \text{NH}_4^+ + \text{NH}_4^+ + \text{SO}_4^{--}$ .

From the examples given it may be seen that ions may be either single atoms or groups of atoms, but they differ from the atoms of elemental molecules in having radically different properties because of the electric charges which they hold when in the ionic form. Hydrogen, for example, has very different properties as an ion than it has as a gas. Oxygen (acid former) was so named because it was once thought that oxygen was necessary for acidity, but it now appears that hydrogen in ionic form is necessary for acidity, and the greater the degree to which an acid ionizes the more pronounced its acid properties. In like manner it appears that hydroxidion is necessary for alkalinity.

The extent to which compounds ionize when passing into solution is dependent upon temperature and the degree of concentration of solution, and varies with the composition of the substance. Such acids and bases as ionize freely are known as "strong acids" and "strong bases," respectively, while those which ionize but slightly are said to be "weak." Salts of "strong" acids with "strong" bases, those of "strong" acids with "weak" bases, those of "weak" acids with "strong" bases all ionize freely; and even those of "weak" acids with "weak" bases ionize quite appreciably. With but few exceptions, salts ionize more freely than the acids and bases to which they are related. Salts of the type  $\text{Me}'\text{X}'$  ionize most freely, those of the types  $\text{Me}_2'\text{X}''$  and  $\text{Me}''\text{X}_2'$  ionize less freely, and those of the type  $\text{Me}''\text{X}''$  still less for a given concentration of solution.

In concentrated solutions we may have both molecules and ions, the former predominating; in rather dilute solutions we may have both, with the ions predominating; while in very dilute solutions we may have ions only. The extent to which a compound dissociates when dissolved in a dissociating solvent may be determined from the freezing point, the boiling point, the osmotic pressure and the electrical conductivity of the solution as compared with the same

constants for the pure solvent. The conductivity method is the one most used, though results calculated from all agree closely in practice.

A tabular arrangement of some of the common acids, bases and salts, with data showing the degree to which they ionize under similar conditions is instructive. The figures given show percentages of dissociation at 18° C., and, except where otherwise indicated, are for normal ( $N/1$ ) aqueous solutions:

Substance.	Per Cent. Dissociated.
Nitric Acid (62%).....	9.0
Nitric Acid (6.3%).....	83.0
Sulphuric Acid (.5%).....	0.7
Sulphuric Acid ( $N/1$ ).....	51.0
Hydrofluoric Acid.....	7.0
Acetic Acid.....	9.4
Potassium Hydroxide.....	77.0
Sodium Hydroxide.....	73.0
Ammonium Hydroxide.....	0.4
Disodium Phosphate ( $N/32$ ).....	83.0
Ammonium Chloride.....	74.0
Sodium Chloride.....	67.6
Sodium Sulphate.....	44.5
Zinc Sulphate.....	24.0
Copper Sulphate.....	22.0
Mercuric Chloride.....	1.0
Carbonic Acid ( $N/10$ ).....	0.17
Phosphoric Acid ( $N/2$ ).....	0.17
Boric Acid ( $N/10$ ).....	0.01
Calcium Hydroxide (saturated solution).....	90.0

Most chemical action, possibly all chemical action, is between ions and not molecules.

Hydron holds its charge less firmly than most cations of bases. This explains the action of acids on metals where hydrogen gas is liberated as the metal goes into solution. Hydron loses its charge and becomes free hydrogen while the metal takes the charge, becomes ionic and passes into solution.

Example:  $\text{Zn} + \text{H}^+ + \text{H}^+ + \text{SO}_4^{--} = \text{Zn}^{++} + \text{H}_2 + \text{SO}_4^{--}$ .

Hydroxidion  $\text{OH}^-$  holds its charge less firmly than almost any other anion except chloridion ( $\text{Cl}^-$ ), bromidion ( $\text{Br}^-$ ), iodidion ( $\text{I}^-$ ) and their like.

Highly concentrated acids, even the so-called "strong" acids—hydrochloric, nitric and sulphuric—have little or no action on metals



which are easily attacked by dilute solutions of the same acids. A familiar example is the behavior of sulphuric acid on iron. The diluted acid attacks the metal readily with the liberation of hydrogen gas, while the highly concentrated form of the acid has so little action on the metal that iron is used in the construction of tanks, tank cars and other containers for the storage and transportation of this acid. The same is true of hydrochloric and nitric acids.

Reference has been made to the fact that the extent to which a compound dissociates in solution may be determined by conductivity methods. The more ions in a given solution the better it will conduct the electric current. As a solution containing molecules and ions is diluted its conductivity increases until a certain point is reached, complete ionization, after which the conductivity decreases with further dilution, as the number of ions in a unit volume of solution becomes less.

The relative conductivity of several substances in solution are here given for study.

Gram-Molecules in 1000 Gms. Water.	HNO <sub>3</sub>	HCl	KCl	NaCl
1.00.....	2770	2780	919	695
0.50.....	2991	3017	958	757
0.10.....	3225	3244	1047	865
0.05.....	3289	3330	1083	895
0.01.....	3395	3416	1147	962

Reference to the table shows that solutions of acids are much better conductors than solutions of salts of the same concentration, and it has been shown that bases give solutions intermediate in conductivity. Among the electrolytes "strong" acids are the best conductors, with "strong" bases next and salts the slowest. This is explained when one compares the relative velocities of their ions, hydron being the swiftest, hydroxidion next in speed, and other ions slower, in any given solvent and under any given driving force. Compare the following figures which show the relative velocities of several common ions at 25° C.:

H ion, 325; OH ion, 170; Na ion, 49.2; K ion, 70.6; Cl ion, 70.2. The velocity of an ion in any given solution is independent of the nature, number or condition of other ions present in the same solution, an important fact in hydrogen-ion concentration determinations.

While metals are better conductors at high temperatures than at low temperatures, the reverse is the case with electrolytes. It

is believed by some that at absolute zero conductivity would be infinite.

The neutralizing value (strength) of acid and base is usually determined by titrating a solution of one with a standard (so-called "Volumetric") solution of another of opposite chemical character, the point of neutrality being determined, more or less accurately, by having in the solution which is being titrated a small quantity of a so-called "indicator," usually an organic compound, which shows by change of color the presence of a slight excess of the reagent being used for neutralization.

In all cases of neutralization, whether of an acid by a base or a base by an acid, the reaction takes place by reason of the H ions from the acid combining with the OH ions from the base to form undissociated water, while the anions from the acid and the cations from the base remain, at least in part, as ions in solution. When the solvent is removed, generally by evaporation, these ions combine to form molecules of a salt. As one writer has expressed it:

"In every case of neutralization the products are: 1. Undissociated water. 2. A solution containing cations from the base and anions from the acid. 3. Energy in the form of heat."

With strong acids and strong bases in dilute solution the heat from gram-equivalents of each is 13,700 calories—the heat of combination of one gram of H ion with seventeen grams of OH ion. With the acid or base, or both, weak, the heat liberated may be greater or less than 13,700 calories, heat being taken up in some cases, and given off in other cases, in the ionization of molecules which were undissociated when the process of neutralization was begun.

It has been estimated that three-fourths of all known chemical reactions involve the formation of water, and if these were eliminated from our chemistry we would have but little on which to build a science.

There are two theories with reference to what takes place when an organic indicator changes color in acidimetry and alkalimetry.

The one held by Ostwald is that, under one set of conditions, only molecules of the indicator (with its characteristic color) exist in the solution, while, under opposite conditions as to acidity or alkalinity, a salt of the indicator (formed when the excess of reagent is added) undergoes ionization, the new color being that of a complex ion from this salt. Most indicators are weak acids, and accord-

ing to this theory, the color of their neutral or acid solutions is due to molecules of the indicator, while in alkaline solutions their wholly or partly ionized salts exist, with a different color because of these ions.

The other theory, advanced by Stieglitz, and quite generally accepted by physical chemists, is that in passing from acidity to alkalinity, or *vice versa*, there is a chemical change within the molecule of the indicator to form a new compound which, structurally, differs from the original substance only in the arrangement of atoms and atomic groups (a so-called "tautomeric compound"). Generally the "lactoid" group  $\text{—C}_6\text{H}_4\text{—}$  group becomes the "quinoid" group  $\text{=C}_6\text{H}_4\text{=}$ , or *vice versa*, one of these being called a "chromophoric" group. The compound with the lactoid group has one color, that with the quinoid group another color.

Of the rather large number of substances which may be used as indicators we find that few of them change color at the same stage of acidity or alkalinity, hence cannot be used interchangeably in many processes involving neutralization, particularly those where results approaching exactness are desired.

Hildebrand<sup>1</sup> gives in tabular form the relative values of a lot of those in more or less general use, the values being expressed in terms of hydrogen-ion concentration, explained more fully further on in this paper. From this table the following data were taken:

Cochineal. Yellow at  $10^{-4}$ , yellow-pink at  $10^{-5}$ , lilac at  $10^{-6}$ .

Litmus. Red at  $10^{-5}$ , red-violet at  $10^{-6}$ , violet at  $10^{-7}$ , blue at  $10^{-8}$ .

Methyl Orange. Rose at 1.0, orange at  $10^{-4}$ , yellow at  $10^{-5}$ .

Phenolphthalein. Colorless at  $10^{-8}$ , red at  $10^{-9}$ .

Methyl Red. Red at  $10^{-3}$ , pink at  $10^{-5}$ , yellow at  $10^{-6}$ .

Inasmuch as  $10^{-7}$  is the figure for neutrality and those with indexes of less than  $-7$  indicate acidity (increasing as the index decreases) and those with indexes higher than  $-7$  indicate alkalinity (increasing as the index increases), it will be seen at a glance that indicators do not generally change color at a neutral point, but rather, at a definite hydrogen-ion concentration peculiar to each indicator.

Since these differences exist, since, as has been shown, different substances ionize in different degrees, and since it is not always pos-

<sup>1</sup> Jour. Am. Chem. Soc., 35: 856, 1913.

sible easily to determine just what particular acidic or alkaline compound may be present in a given solution to govern one in the choice of indicator to be used, it is not surprising that methods by which the hydrogen-ion concentration of a solution may be determined electrometrically should be receiving so much attention as they are in certain quarters and among certain workers at the present time. There are other reasons, which we expect to give in this paper, for the favorable reception that electrometric processes are getting.

Before going into any explanation of electrometric methods for determining the hydrogen-ion concentration of solutions it is pertinent to look into some of the facts underlying them.

Theoretically, it is impossible to get or make any substance absolutely pure, since every substance is soluble in some degree in every other substance with which it comes into contact, hence absolutely pure water is not obtainable. By rather elaborate methods of purification water has been prepared so nearly pure that a millimeter cube of it was calculated to give the same resistance to the passage of an electric current through it as would a copper wire a square millimeter in cross section and long enough to encircle the earth at the equator a thousand times. Such water, called conductivity water, has a specific conductivity of about  $10^{-6}$ , and is sufficiently near pure to be used in making solutions for hydrogen-ion determinations. Water ionizes according to the following equation:

$\text{H}_2\text{O} = \text{H}^+ + \text{OH}^-$ , but the degree of ionization is very slight, so that absolutely pure water at  $22^\circ$  to  $23^\circ$  C. is estimated to contain H ions of a concentration expressed at  $10^{-7}$  and OH ions of the same concentration, which corresponds to one gram of H ions and 17 grams of OH ions in ten million liters. This is equivalent to a ten-millionth normal solution of either acid or alkali (N/10,000,000).

In any solution containing ions from a dissociated compound the product of the concentration of the positive ions (cations) and the concentration of the negative ions (anions) is a constant. The constant at  $22^\circ$  C. for pure water is, accordingly,  $10^{-7}$  (for H) times  $10^{-7}$  (for OH), or  $10^{-14}$ .

If to a solution containing ions of a certain kind there be added a substance yielding ions of the same kind, the ionization of the compound which furnished the original ions will be "pushed back" sufficiently to make the product of the new concentrations the same

as the product of the original concentrations. This is in accord with the so-called "law of mass action."

This behavior of the ions may be likened to a social party attended by men and women going there in couples and "dissociating" as soon as they come together in the place where the party is being held. The number of chances each man has of meeting a different woman is *one* multiplied by the number of women, and the total number of chances of meetings, differing as to the personnel of the people concerned, is determined by multiplying the number of men by the number of women. Let us suppose there are four couples in the party—four men and four women. The number of different meetings possible will be 4 times 4, or 16. Now let us suppose that the party is increased by the appearance of six other women each carrying a dog, and that two of the first four women (who do not like dogs) take their escorts and go home. There will be left 2 men and 8 women and the different combinations possible will be 2 times 8, or 16, as before. The number of couples will have been reduced from four to two, the *man concentration* decreased by half, and the woman concentration increased.

Now, let us substitute four molecules of dissociated water in a given volume for the four couples, and we will have four H ions and four OH ions. If we add to the water sufficient sodium hydroxide to give us six molecules of dissociated NaOH we will be introducing six Na ions and six OH ions, and two molecules of water will be formed from two ions each of H and OH, leaving only two of the original H ions. The solution will now be alkaline from the excess of OH ions, but its strength may be stated in terms of hydrogen-ion concentration (acidity), being relatively less acid than water, through having in it fewer H ions (the cause of acidity) than originally.

The following table shows various methods in use for stating the strength of solutions of acids and alkalies in terms of normality and hydrogen-ion concentration. A normal solution of an acid represents one gram of H ions in one liter, while a normal solution of an alkali represents seventeen grams of OH ions in one liter. In the table the first three columns show the common fraction and decimal fraction methods, respectively, for indicating strengths, the third column numbers being abbreviated forms of those in the second column, while the fourth and fifth columns show two forms in use for expressing the H-ion concentrations.

$N/1$ (acid)	1.0	1.0	1.0	1.0
$N/10$	0.1	0.1	$10^{-1}$	$PH_1$
$N/100$	0.01	0.01	$10^{-2}$	$PH_2$
$N/1000$	0.001	0.001	$10^{-3}$	$PH_3$
$N/10000$	0.0001	0.0001	$10^{-4}$	$PH_4$
$N/100000$	0.00001	0.00001	$10^{-5}$	$PH_5$
$N/1000000$ (acid)	0.000001	0.00001	$10^{-6}$	$PH_6$
$N/10000000$ (neutrality)	0.0000001	0.00001	$10^{-7}$	$PH_7$
$N/1000000$ (alkali)	0.000001	0.00001	$10^{-8}$	$PH_8$
$N/100000$	0.00001	0.00001	$10^{-9}$	$PH_9$
$N/10000$	0.0001	0.0001	$10^{-10}$	$PH_{10}$
$N/1000$	0.001	0.001	$10^{-11}$	$PH_{11}$
$N/100$	0.01	0.01	$10^{-12}$	$PH_{12}$
$N/10$	0.1	0.1	$10^{-13}$	$PH_{13}$
$N/1$ (alkali)	1.0	1.0	$10^{-14}$	$PH_{14}$

It will be noted that half of the numbers given in the first three columns represent acidity, and the other half represent alkalinity. The data given in the last two columns represent relative acidity, an  $N/100$  solution of alkali, for example, having a hydrogen-ion concentration of  $PH_{12}$ , or  $10^{-12}$ .

If two electrodes of the same metal are placed in solutions of the ions of the same metal in different concentrations,  $c_1$  and  $c_2$ , respectively, and these solutions are placed in electrical contact, either through a porous partition or by means of a siphon, or even separated by gravity alone, there exists between the two electrodes a difference of potential, expressed fairly closely by the formula,<sup>1</sup>

$$E = 0.000198 \, T/n \log c_1/c_2$$

where  $E$  denotes the difference of potential,  $T$  the absolute temperature and  $n$  the valence of the ions of the metal in solution. At room temperature, about  $18^\circ \text{C.}$ , the formula becomes

$$E = 0.058/n \log c_1/c_2. \quad [0.000198 \times (273 + 18) = 0.058.]$$

If the metal is silver (when  $n = 1$ ) and if  $c_1$  and  $c_2$  are 0.1 and 0.001 normal, respectively, then  $\log c_1/c_2 = \log 100$ , or 2, and  $E = 0.116$ . Conversely, when  $E$  is measured, either concentration can be easily calculated if the other is known. It is thus possible to determine quite accurately even very small ionic concentrations, and such determinations as the solubility of the silver halides may be easily made.

<sup>1</sup> Hildebrand, *Jour. Am. Chem. Soc.*, 35: 848, 1913.

Now the same principle can be applied to the determination of hydrogen-ion concentration (acidity or alkalinity), if for electrodes we use a noble metal, like platinum or palladium saturated with hydrogen gas under definite pressure. These electrodes are usually of platinum or gold in thin sheets previously covered with platinum black by electrolytic methods, and so disposed in a glass holder that they can be kept saturated with the gas. Their action is the same as if the hydrogen were in solid form. If we use such an electrode dipping into a solution containing normal hydrion so that  $c_1 = 1$ , and measure the difference of potential between it and another similar electrode dipping into a solution of which the hydrogen-ion concentration is unknown, the two solutions being connected, let us say, by a siphon containing concentrated potassium nitrate or chloride solution, then the unknown concentration and the difference of potential are related by the expression

$$E = 0.058 \log 1/c.$$

In practice a calomel electrode (consisting of pure mercury in contact with a saturated solution of  $\text{Hg}_2\text{Cl}_2$ ) is used in place of one of the hydrogen electrodes. This involves the making of a correction in the final calculations, but this disadvantage is more than balanced by the advantages to be gained by the substitution. For measuring hydrogen-ion concentrations a calomel electrode, a hydrogen electrode and a potentiometer for measuring the voltage between them are employed.

We have seen that all acids contain hydrogen atoms which when the acid is diluted with water, become hydrogen ions. Some acids, the so-called "strong" acids, are more highly dissociated in a solution of given concentration than are others, or, in other words, yield solutions of greater hydrogen-ion concentration. The organic acids are, relatively, "weak" acids, but differ from each other quite widely at times in this respect. In many vital processes, such as, for example, those in which chemical changes are brought about by the presence, in solution or suspension, of ferments or bacteria, the rapidity of the action, the nature of the substances formed, and other factors, are apparently dependent in large part upon the hydrogen-ion concentration of the medium in which the changes are taking place, rather than upon the total acidity or alkalinity, as was for a long time supposed to be the case. The total acidity of a solution depends upon the amount of acidic hydrogen present

both as hydron and in undissociated molecules of acid, and the total alkalinity of a solution depends, likewise, upon the amount of hydroxyl (OH) present both as hydroxidion and in undissociated molecules of base. Hydrogen-ion concentration, on the other hand, depends upon the H ions alone, and its value for a given solution may be low when compared to the total acidity as obtained by titrametric methods. It is clear, then, that volumetric methods for determining acidity of a medium in which the concentration in H ions is the important factor have practically no value. This probably accounts for many of the discordant results often obtained, by workers in bacteriological fields, for instance, where relative acidity or alkalinity have so much to do with the success or failure of such a process, for example, as that of growing a culture of a certain micro-organism on some particular culture medium. Two lots of culture media may have the same degree of acidity or alkalinity, as determined by volumetric methods, and may seem the same in other particulars, yet one may serve admirably for growing cultures of a certain micro-organism, while the other is worthless. Often it has been found that two such media differed quite radically in hydrogen-ion concentration, and those workers who are preparing their media in such a manner as to make them approximately uniform in the matter of hydrogen-ion concentration seem to be obtaining concordant results more often than formerly.

The hydrogen-ion concentration of a solution may be determined fairly accurately by colorimetric methods, in which, by adding to portions of the solution under examination various indicators, color changes are brought about, which are dependent upon the nature of the indicator and its sensitiveness to the concentration of H ions present. Other methods have been used, but, next to conductivity methods, the colorimetric method is preferred, though it leaves much to be desired in processes where results closely approaching accuracy are sought.

Measurements<sup>1</sup> of electrical conductance can be employed in the determination of the point of neutralization of a base by an acid, or an acid by a base; and the method is of especial importance when dealing with colored or turbid solutions, in which the change of color of an indicator would be more or less masked.

When a solution of a strong acid is added to a solution of an alkali the conductance of the latter solution decreases, owing to the dis-

<sup>1</sup> Findlay: "Practical Phys. Chem.," p. 199. Longmans, Green & Co., 1914.



appearance of hydroxidion and its replacement by the less mobile anion of the acid: but when all the hydroxidion has been removed by combination with hydrion from the acid added, then any further addition of acid causes the conductance to increase, owing to the addition of the solution of the very mobile hydrion. Since the velocity of hydrion is much greater than that of any other ion, the presence of a slight excess of free acid causes a marked increase on the conductance. Similar results are obtained when a solution of a base is added to a solution of an acid, provided both base and acid are strong. When the acid is weak it must be added to the alkali, which in this case must be a strong base.

The advantages that conductivity methods have over colorimetric methods are chiefly these:

1. No great skill is required, as delicate galvanometers are used which give an accurate measurement of potential.
2. No complicated calculations are necessary.
3. The personal equation counts for almost nothing, and color blindness is no bar, as in the case of the use of indicators.
4. Precipitates, opacity or colors of solutions do not interfere.
5. The method is fundamental, as colorimetric methods are referred to it.
6. Potentiometers are now made which cover the entire range of PH values while any one indicator is useful over a limited range only.

Conductivity methods are largely replacing volumetric methods in many laboratories connected with large industries for making determinations other than those involving neutralization. Particularly is this the case with determinations depending upon oxidation and reduction, as in many operations connected with iron and steel analysis. The determination of the percentage of chromium, manganese, vanadium and carbon in steel and in presence of one another are relatively simple matters, with these advantages over volumetric methods:

Accuracy. If chromium is present in steel to the extent of 20 per cent., it may be determined to within 0.1 per cent.; if present to extent of 0.2 to 0.3 per cent. it may be determined to within 0.01 per cent.; if less than 0.2 per cent. it may be determined to within 0.002 to 0.003 per cent.

2. Rapidity, where a large number of determinations are to be made.
3. Non-interference of color or precipitate.
4. Sharp end-points are usually obtained.
5. Little or no chemical training is needed on the part of the operator.

Other determinations that have been made with apparatus based upon conductivity are: Magnesium in presence of calcium, ferrous iron in presence of ferric iron, patent flour in admixture with straight flour and "red dog," the solubility of sparingly soluble salts (such as the haloid salts of silver, barium sulphate, lead sulphate, etc.), the hydrolysis of weak acids and weak bases. Conductivity methods of analysis are relatively new but, as they become better known, promise to supplant many of the older and slower methods of gravimetric and volumetric analysis, particularly in laboratories connected with industrial establishments. Several firms are now supplying complete apparatus for special kinds of determinations, and improvements are being constantly made on what first appeared on the market.

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## COMPOSITION POWDER.

BY EDWARD J. HUGHES, P.D.,

PHILADELPHIA, PA.

In order to determine just what Composition Powder is, we should go over some of the complicated references dealing with this preparation and extending back to its origin nearly a century ago. For a long time Composition Powder was a popular and widely used remedy. At present this title is recognized by the National Formulary (4th. Rev.) as a synonym for Pulvis Myricae Compositus or Compound Powder of Bayberry. The N. F. requires that it shall be made by mixing together twelve parts of powdered bayberry root bark, six parts of powdered ginger and one part each of powdered capsicum and powdered cloves.

A search through the literature reveals a great variety of formulas for Composition Powder, with little or no comment as to their

source and with no uniform relation to each other aside from the fact that they are all "hot" to the taste. It is also found that the N. F. Latin and English titles for this preparation were previously employed by the Eclectics in naming a mixed powder of somewhat different character.

Composition Powder originated with the work of Dr. Samuel Thomson, who, according to Gorton's History of Medicine (1910), was the founder of a medical sect known as Botanic physicians. Dr. Thomson is said to have believed in the maxim that "heat is life and cold is death." It is only necessary to read over a few of the formulas employed by him to realize that they were in keeping with his doctrine.

The first mention of Composition Powder is found in Thomson's "New Guide to Health," published in Boston in 1825. The Formula given in this work under the title "Composition or Vegetable Powder" is as follows: Bayberry Root Bark 1 lb., Hemlock Bark 1 lb., Ginger 1 lb., Cayenne 2 ozs., and Cloves 2 ozs. Why Dr. Thomson called this mixture Composition Powder is not stated. In his description he refers to the mixture as "this composition" and suggests its use for acute colds, in the early stages of disease and as a sudorific. It is possible then that he applied this title for the want of a better one and because of the fact that the preparation is a putting together of composite parts or medicines to produce a desired effect.

In a later edition of Dr. Thomson's work (1835) this formula was changed by omitting the hemlock bark. It is of interest to note that this formula now corresponds, in ingredients and proportions, to the one adopted by the National Formulary. In his "Materia Medica and Anatomy," 13th edition (1841), Dr. Thomson enlarged upon the subject by publishing three formulas under the heading "Composition Powder" each one containing bayberry, ginger, cayenne and cloves in varying proportions. The formula given for the first of these three preparations agrees with the formula of 1835 and with the formula of the N. F. The second and third preparations, besides differing in proportions, contain in addition some poplar, hemlock, or red or white oak bark.

Beach's "Family Practice" (1842), published a formula for a compound powder of bayberry using the title "Cephalic Powder." This preparation was composed of equal parts of bayberry root bark, bloodroot and snuff, and was said to be useful for catarrh and headache.

Cephalic Powder again appears in King's American Dispensatory (1852) but with the snuff omitted from its formula. Here the scientific title "*Pulvis Myricae Compositus*" is first employed, the old title "Cephalic Powder" being retained as a synonym.

In the 1909 edition of King's "Dispensatory" we again find Cephalic Powder under the title "*Pulvis Myricae Compositus (Eclectic)*" or, Compound Powder of Bayberry. It is also pointed out in this work that this powder should not be confused with "Composition Powder" bearing the same title.

Dick's "Encyclopedia" (1872) publishes a formula for Thomson's Composition Powder which does not agree with the one accepted by the National Formulary but which does correspond, practically, with the third formula given by Thomson under "Composition Powder" in his "*Materia Medica*" of 1841.

The first edition of the National Formulary, published in 1888, accepted the formula for Composition Powder as given by Thomson in his works of 1835 and 1841, and applied to it the Latin title "*Pulvis Myricae Compositus*." Compound Powder of Bayberry was the, English name employed and the old title, "Composition Powder," was made the synonym. These titles and formula have been carried through all succeeding revisions of the N. F. without change.

Some idea of the use and misuse of the name "Composition Powder" can be gotten by an inspection of some of the pharmaceutical formularies. For example, the Pharmaceutical Journal Formulary of London (1904) publishes a group of thirteen formulas, differing not only in ingredients but in proportions used, all entitled Composition Powder. In comparing these formulas, briefly, it was found that all of them contained capsicum and ginger, eleven contained cloves and only nine contained bayberry bark which is the principal ingredient in the Thomsonian Composition Powder and from which the Latin and English titles are taken. The other ingredients in these formulas were chiefly cinnamon bark and laurel berries.

The Era Formulary of 1914 gives six formulas for Composition Powder not one corresponding exactly to the Thomsonian formula recognized by the National Formulary. Several other references showed contradictory formulas which are unnecessary to discuss in detail at this time.

To summarize briefly, Composition Powder originated with the work of Dr. Samuel Thomson in 1825 or earlier. It became popular and found its way into many of the works on materia medica and

pharmacy, its formula in many cases becoming quite elastic. It is now recognized by the National Formulary, the formula here being identical with formulas published by Dr. Thomson in his works of 1835 and 1841. In naming this preparation, however, the N. F. applied a title which had already been employed in Eclectic practice for another preparation known as "Cephalic Powder."

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## THE BUSINESS POSSIBILITIES OF MANUFACTURING IN THE RETAIL DRUG STORE.<sup>1</sup>

BY GEORGE M. BERINGER, JR., P.D.,

CAMDEN, N. J.

In the matter of manufacturing, the retail druggists of the United States might be divided into two classes: those who prefer to devote all their energies to salesmanship, and, hence, make practically nothing, and those who make a few of the commoner preparations and specialties, but draw the line at certain preparations which tradition, more than fact, says can be made more cheaply by the large manufacturer. Those of the first class buy Brown Mixture, Chalk Mixture, Syrup Wild Cherry and Solution Magnesium Citrate. They even buy five- and ten-cent packages of Epsom Salt and sell them again—as far as the contents go—sight unseen! These are the men who continually decry the advancements in Pharmacy, who would turn our colleges into mere schools of salesmanship, yet they, themselves, violate the first principle of modern salesmanship in that they know nothing about the goods they sell. The second class, I fear, are less numerous than the first. They are surely, fundamentally, better merchants than their pseudo-successful brethren of the first class, and would probably be more successful were they but fully alive to the business possibilities that their manufacturing offered.

The trouble is, that the average druggist of all classes thinks only of his profit as the difference between the cost and the selling price. If business were so simple, we would all be merchant princes. However, there are a number of factors which make the problem

<sup>1</sup> Read before the Commercial Section of the American Pharmaceutical Association, New York City, August, 1919.

more complex. It is my purpose to bring before you a few of the factors that are only too often ignored.

Suppose that A and B, competitors, have each an "own name preparation" of the same type prepared for them by the same manufacturing house. Of course, that house offers a selection of designs for the packages, so that each preparation may appear somewhat different externally. A customer, who happens to purchase packages of the article from each, realizes that the contents are the same. The name of neither competitor on that article has given him any advantage. But, let us further suppose that B has manufactured the article himself and has worked certain ideas of his own into the preparation proper, giving it a distinctive character. The chances are that the customer who divides his purchases between A and B finds that distinctive characteristics of B's product pleasing or helpful to him. B has won the first point in the game of competition. He has established individuality, and individuality means "good will," and "good will" means possibly a hundred thousand dollar business for B against a ten thousand dollar business for A, though both may have been of equal professional ability at the start.

Now, I know some one is waiting to say, "I'll wager B's product cost him more to manufacture, on his small scale, than A's cost him to buy." Let us grant, for the sake of argument, that this is true. Say A paid fifteen cents for his article and sold it for twenty cents. Say B produced his preparation at a cost of seventeen cents and sold it for twenty-five cents. A's gross profit was, in round figures, 33%, B's 47%. But, if B fully appreciated the value of his improvement of the product, and had the proper business acumen, he probably asked thirty or thirty-five cents for his article and got away with it. You see, there is some reason back of that hundred thousand dollar business. The "cashing in" on that "good will," anyhow.

The average man looks upon the immense plant of the manufacturer with its vast accumulation of special machinery, its expensive research workers and its brilliant sales force and immediately develops a case of "cold feet," in so far as manufacturing for himself is concerned. He forgets that the brilliant sales force does not have to figure in the overhead he carries upon his small operation. He forgets that the expensive research workers, with all respect for their contributions to the advancement of science, are as much a part of the advertising department as an aid to the manu-

facturing department of such concerns, and that he can be his own research worker with a versatility not equalled by these specialists. He forgets that his ingenuity and skill can overcome, in many cases, the vast accumulation of special machinery, and that an immense plant means an immense "up-keep."

Many stores have certain hours of the day during which very little business is transacted. In this time the employees have but few tasks. This waiting time might be employed in manufacturing with actual saving of overhead expense. I am not advocating "slave driving." It is a well-established fact that machinery will deteriorate most rapidly when lying idle. The same is true, in a way, of human machinery, and druggists' assistants employed pleasantly, sanely but continuously will be more efficient in every way than those allowed to stand idle during slack time. There is another point that here suggests itself. No salesman can sell goods with a "snap" equal to that of the man who makes them and therefore knows all about their intrinsic value.

The advantage of quality should, and often does, rest with the product of the small retail manufacturer. The workman in the large laboratory, to whom the real manufacturing is intrusted, is usually a mere laborer in whose eyes the work is only mechanical routine. The workman in the store is the proprietor and his clerks, men of better training and intelligence and with a more active interest in the work. As an instance of this, I have seen fluid extracts manufactured by a retailer which were far superior in brilliance, aroma and body to many turned out by the large manufacturer with his advantage of stills and vacuum apparatus. That this advantage may be capitalized has already been pointed out.

Certain classes of preparations, such as coated tablets and pills, which require expensive machinery; fluid extracts, in general, which require the recovery of quantities of alcohol; and biologics and alkaloidal extracts, which require expensive control and assay processes, are, in the main, beyond the reach of the small manufacturer to produce. Yet, even here, are exceptions.

While coated tablets and pills are practically impossible of production, economically, on a small scale, the same is not true of plain compressed tablets, tablet triturates and hypodermatic tablets. While the cost of these on a small scale would be somewhat higher, such manufacture permits of supplying the local demand with products of superior quality as regards solubility and disintegration,



since it is not necessary to make the tablets hard enough to withstand the extra strain of distant transportation. Another factor in regard to tablets is the ability of the small manufacturer to supply limited quantities of the special formulas for which there is always a demand among his local physicians. The cost of the necessary utensils need not be very great. A first-class, hand-power tablet compressing machine, with a reasonably complete assortment of dies and punches, can be secured for less than fifty dollars. A set of hard rubber molds for tablet triturates and hypodermatic tablets can be secured for from five to ten dollars, depending on the number of molding plates desired in each set. In any case, this tablet equipment should be part of every complete prescription department. I might observe that the man who makes a line of tablets is getting a better knowledge of the physical properties of drugs than can be had in any other way.

Among fluid extracts, there is one which no self-respecting druggist should buy, that is, Fluid Extract Cascara. In its manufacture there is no waste of alcohol and the process is simple. The cost of production figures about as follows:

		Per Pint.		Per Gallon.
Ground Cascara Bark.....	1 lb.	.30	8 lbs.	2.40
Alcohol.....	4 fl. oz.	.20	1 qt.	1.50
Time and fuel.....		.50		1.25
Container.....		.10		.25
		<hr/>		<hr/>
		\$1.10		\$5.40

Actual cost will in most cases average a little under these figures. Manufacturers quote from \$1.35 to \$1.80 per pint. The manufacturer quoting the lower figure per pint, names \$6.50 as his best price per gallon. It might also be mentioned that Fluid Extract Licorice is in the same class from a manufacturing standpoint.

The retail druggist who manufactures at least some portion of his own preparations has one advantage which is rarely ever considered, that is, the ability to meet emergencies. During the recent influenza epidemic, both manufacturers and wholesalers in many sections of the country were from two to three weeks behind in the filling of orders. Common preparations like Spirit of Nitre were almost unobtainable. I know of one druggist who made his own Ethyl Nitrite when he found that the market was bare of that substance. It would not have paid him under ordinary circumstances

but the needs of humanity at that time were paramount to the expense of production. Then too, one can imagine the prestige he gained when his customers told others, "If you can't get it anywhere else, you can get it at 'So and So's.' " The druggist who manufactures, even in a small way, has apparatus and raw material on hand that, otherwise, he would not have, and, when the need arises, can turn them to account. Thereby, he not only reaps a just financial reward, but receives the satisfaction of having helped his fellow men.

Business is a complex problem, never more so than at present. A multitude of little-considered factors contribute to the success or failure of those engaged in it. We are only too apt to say that because two and two make four we have found the correct answer to the problem. However, if another figure has been omitted from the column, it avails us nothing that our answer was, in so far as it went, correct.

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## STATUS OF LEGISLATION ON ARMY AND NAVY PHARMACISTS.

BY E. FULLERTON COOK, PH.M.,

PHILADELPHIA, PA.

The Secretary of the National Pharmaceutical Service Association has had the opportunity on several occasions recently to confer with Surgeon-General Ireland, of the Army and Surgeon-General Braisted of the Navy, concerning the details of proposed pharmaceutical work in the reorganized military service.

It is gratifying to learn that Dr. Ireland's plan for a Medical Service Corps, which is to assume work which is not strictly medical, but connected with the medical corps, has met with the approval by both the Committees of the House and the Senate, and by the General Staff of the Army, and is incorporated as a part of the new Army bill about to be submitted to Congress. It will be remembered that Dr. Ireland agreed to have a *pharmaceutical section* in this Medical Service Corps, in which a limited number of pharmacists would be commissioned. This favorable status for the proposed

Service Corps practically assures its enactment into law, and in the establishment, for the first time, of proper pharmaceutical representation in the United States Army. The original suggestion of Dr. Ireland that a five-year enlistment period be the pre-requisite for securing commissions, was criticized by many pharmacists, and it was pointed out that those men who were best competent to administer the activities of such a corps, would never be willing to serve as privates for five years to secure a commission.

In the recent conference with Dr. Ireland and Colonel Darnall, these facts were pointed out and were appreciated by the Surgeon-General, and it was agreed that modifications would be asked for in the bill establishing the Medical Service Corps. The suggested modifications consist of the change of the five-year enlistment to three years as a pre-requisite for commissions. Secondly, a recognition by the Surgeon-General's office of previous military training, or suitable technical training as a part of this three-year enlistment. In other words, a commission to be granted in less time than three years, if the training previously received justified such appointment. Under similar rules in the Navy, commissions have been earned in a short time by men who have had suitable training before enlistment and it is proposed to follow the same plan in the Army.

Another fact which will be gratifying to pharmacists was the interest expressed by Dr. Ireland in the establishment of a reserve officers' training school, for the prospective Reserve Medical Service Corps, which, it is hoped Congress will authorize. The plan would be to arrange for special training for those graduates in pharmacy who desire to enlist in the Reserve Corps. This would be given in a reserve officers' training school and pharmacists could thus qualify as officers of the reserve corps, and be partially trained for immediate duty and commissions in time of war. Dr. Ireland also expressed the hope that if the Medical Service Corps is authorized by Congress, and the Reserve Corps established (and this he will undertake to organize), that some of the highly trained pharmacists who have had military experience in the recent war will be willing to enlist at once as officers in this Reserve Corps and be placed on active duty in his office to assist in the organization and proper establishment of the pharmaceutical section. This plan would give the Corps at the beginning the benefit of the valuable experience of highly trained men who would probably be willing to devote a few months of their time for the establishment of the corps on a scientific

basis, but without the requirement that they serve longer than necessary for organization. Of course, the details must be more thoroughly developed, but the opportunity is offered pharmacy to establish itself in the Army on the highest possible plane, and Dr. Ireland is very willing to coöperate with pharmaceutical leaders to that end.

The situation in the Navy at this time is as follows: The Bureau of Medicine and Surgery is entirely in harmony with the principle represented by the Darrow Bill, and have done all within their provinces to advance this legislation. Of course, it is understood that naval officials cannot personally advocate legislation, but can only recommend to the Secretary of the Navy what they believe would be to the best interests of their Departments. However, on January 30th, Dr. Braisted, the Surgeon-General, appeared before the House Committee on Naval Affairs concerning the annual appropriation, and this opportunity was taken to secure his testimony concerning the Darrow Bill. He gave the members of the committee his hearty endorsement of the principles involved in this bill and explained the subject in detail. Every member of the committee had previously been interviewed and promised to give it their careful consideration.

The Darrow Bill has recently been submitted to the Bureau of Navigation, which must pass upon all suggestions for new commissions, and some opposition has been encountered. It is hoped that this may be overcome, as Dr. Braisted has sent a comprehensive brief to Admiral Washington, Chief of the Bureau of Navigation, setting forth the importance of establishing permanent commissions in the Hospital Corps, and presentations have been made by others to Admiral Washington, and he is giving the matter his consideration. It may become necessary to enlist the personal interest of every Congressman in this bill and pharmacists of the country should urgently write at this time to their representatives urging that they support the Darrow Bill.

In a conference with Admiral Washington, several alterations in the original draft were found to be desirable, but these can readily be incorporated in the committee. They consisted of the change in rating so that instead of Captain, the highest rating authorized would be Lieutenant Commander. It was also suggested that "required sea duty" be introduced into the bill and also that it be distinctly indicated that the Hospital Corps is a branch of the

Medical Corps, and not an independent organization. This latter has always been understood, but the bill apparently did not make it entirely clear. These modifications will be brought out at the hearings before the Naval Committee.

## YEAST GROWTH AND ALCOHOLIC FERMENTATION BY LIVING YEAST.\*

BY ARTHUR SLATOR.

The methods used by the physical chemist to measure rates of chemical reactions can be applied to investigate the process of alcoholic fermentation by living and growing yeast cells. The results obtained in this way are valuable, for they not only give new information, but also make it possible to bring into line results obtained by other methods. In this communication yeast growth and alcoholic fermentation are considered from this point of view.

The subject matter may be explained by describing the growth of yeast cells in a nutrient medium, and by pointing out the main factors which determine the rate of growth and rate of fermentation at different stages of the reaction.

Number of cells per Cc.  
Time

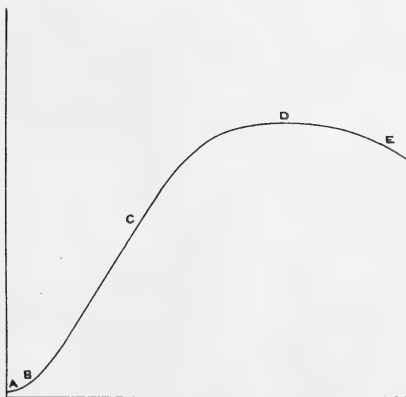


Diagram of Yeast Growth.

A = lag phase in growth; B = logarithmic phase; C = retarded growth;  
D = yeast crop; E = death of yeast cells.

If a trace of yeast is seeded into malt wort, which is a medium

\* Reprinted from *Journal of Society of Chemical Industry*, Oct. 31, 1919.

containing all foods necessary for yeast growth and also large amounts of fermentable sugars, the yeast cells bud and grow. If the number of cells is plotted against the time a curve of the type given in the diagram is obtained.

After a certain initial disturbance (lag-phase) the cells multiply regularly, the number increasing logarithmically with the time. All the usual equations employed to calculate the rate of unimolecular chemical reactions can be applied to yeast growth over this period, if note is made that the reaction is increasing in rate instead of decreasing as is the case with ordinary chemical reactions. There are several methods of measuring this logarithmic constant of growth (K.) or the generation time (G. T.) which is a number inversely proportional to K. ( $G. T. \times K. = \log. 2$ ). Some of them depend on counting yeast cells under the microscope, and others on measuring rates of fermentation from which rates of growth can be calculated.

The results show that when all necessary food is supplied in sufficient concentration yeast cells develop at a rate determined by the temperature and the rate of the yeast used.

Temperature coefficients vary greatly with the temperature. At 25° C. the rate is usually about four times that at 15° C. The shortest generation time so far observed is about 1 hour. The retarding influence of carbon dioxide and alcohol, and the necessity of oxygen for yeast growth can be demonstrated and measured by these methods.

*Lag-phase in Growth.*—If yeast cells from an old culture are introduced into fresh wort a period of quiescence is observed before budding takes place. When growth has once started it continues at the normal rate. A bakers' yeast at 30° C. gave a period of one hour before buds appeared and then all the cells, except the dead ones, budded irregularly during the next hour. Older cultures showed more dead cells but not a longer period of quiescence.

The lag-phase in the growth of bacteria has been examined by Penfold (1914) who used the method of "planting" to estimate the number present, and many important observations were made. Some of the results have been submitted to mathematical analysis by Ledingham and Penfold (1914). The matter has been further discussed (Slator, 1917), but an investigation of the lag-phase in yeast growth (1918), leads one reluctantly to the conclusion

that Ledingham and Penfold's equation is not of general applicability.

There is no doubt of the interest and importance of this period of growth and yeast cells are well adapted for the purpose of further investigation.

*Phase of Retarded Growth.*—As yeast develops in malt wort the first retarding influence which comes into play is that due to carbon dioxide. Continental investigators have rightly laid stress on the preservative action of carbon dioxide; in this country the influence has been recognized, but the effect has been attributed to the exclusion of oxygen rather than to a direct poisoning effect.

The retarding influence of the gas can be detected when the yeast concentration has developed to about a million cells per Cc.

Oxygen is necessary for yeast growth, and lack of oxygen soon makes itself felt and is the main retarding influence when yeast cells develop from a few million cells per Cc. to the maximum growth of about 100 million per Cc.

A. J. Brown (1905) was the first to show that arrest of cell reproduction under these conditions is due to this lack of oxygen. H. T. Brown (1914) further investigated the matter and *inter alia* obtained the important result that yeast growth increases proportionally with the amount of dissolved oxygen initially present in the wort. For the production of  $10^{10}$  yeast cells, 1.7 Cc. of oxygen are required.

Measurements of the logarithmic constants of growth under anaerobic and aerobic conditions have been made. In these experiments malt wort behaved as if it contained a certain amount of combined oxygen available for yeast growth. The results are not in agreement with H. T. Brown's conclusion (1914) that growth under anaerobic conditions is due entirely to oxygen previously absorbed by the yeast.

Alcohol also acts as a retarding agent, but usually growth stops in a fermenting solution before the alcohol concentration is sufficient to have much influence.

*Yeast Crops.*—The cause of the final cessation of yeast growth in malt wort is usually lack of oxygen, but it is evidently possible to arrange conditions under which the yeast crop is determined by other limiting factors.

Lack of fermentable sugar, which also acts as a food for the yeast, may be the limiting factor which finally prevents further growth. A discussion of this typical case will show on what factors yeast crops depend.

During the logarithmic period of growth the yeast growth  $N$  during the time in which  $S$  grams of sugar disappear (by growth and fermentation) is connected with  $K$  the constant of growth and  $F$  the fermentative activity of the yeast by the equation  $N/S = K/F$ . During any other periods of growth the relationship  $\frac{dN}{dS} =$

$\frac{K}{F}$  holds good for small increments in  $N$  and corresponding decre-

ments in  $S$ . We have therefore  $N = \frac{K}{F} dS$ , that is, the yeast crop

from a small seeding is determined by the value of the integral between the limits  $S =$  initial concentration of the sugar to  $S = 0$ . The ratio  $K/F$  and its variation with different sugar concentrations determines the amount of yeast a given medium can produce. If  $K/F$  is constant (which is approximately the case, for both  $K$  and  $F$  are independent) the sugar concentration, except when the solutions are dilute, the growth and the initial sugar concentration will be proportional. H. T. Brown (1914, 226) finds that 2.3 grams maltose disappear when  $10^{10}$  yeast cells are produced.

Yeast growth may cease, owing to the production of large amounts of alcohol. The crop under these conditions is determined by the way the ratio  $K/F$  varies with different concentrations of alcohol, and the same method can be used to calculate the yeast growth. The integral is, in fact, of general application whatever the final limiting factor is.

The ratio  $K/F$  is independent of the number of yeast cells present. It follows, therefore, that with a medium of given composition the total possible growth is a constant, the crop being equal to the sum of the seeding and the growth. A. L. Stern (1901), in a series of careful experiments on the point, has proved this experimentally in the case of a Burton yeast growing in a solution containing glucose, asparagin and mineral salts.

A. J. Brown's previous observation (1892) that large seedings of yeast in wort refuse to bud is contrary to this general conclusion



that the increase should be the same whatever the seeding is. The non-multiplication in this case is probably due to lag in growth and the very rapid accumulation of retarding influences.

Again Stern shows that yeast crops are almost independent of the temperature of growth. The temperature coefficient of growth and that of fermentation over the range of temperature in these experiments are not equal, but approximate closely enough to account for the results obtained.

*Death Rates.*—When yeast growth has finally ceased the cells suspended in the fermented liquid gradually perish. If the liquid is kept free from other organisms a few living yeast cells may still be found after many years' preservation. Very little information regarding death rates of yeast cells is available, but experiments with bacteria show that micro-organisms under unfavorable conditions usually perish at a logarithmic rate (H. Chick, 1908, 1910).

In investigating alcoholic fermentation at high temperatures or in the presence of poisons, death rates and rates of inactivation come prominently into consideration. The process of pasteurization, the preservation of pitching yeast and pure cultures of yeast depend on death rates which have not yet been investigated.

*Growth and Fermentation.*—The main factors which determine the rate of fermentation during any of these periods are the number of cells present, the fermentative activity of the yeast and the temperature. The rate of fermentation is independent of the sugar concentration except in dilute solutions. Sugar concentrations, therefore, come into consideration only at the end of fermentation.

Maltose, the principal sugar in malt wort, is hydrolyzed sufficiently rapidly by culture yeasts to supply adequately the yeast cell with glucose. Dextrin is not fermentable by yeast, but there exist in malt wort substances intermediate between dextrin and maltose which are hydrolyzed slowly by yeast and subsequently fermented. Little is known of the rate of fermentation of such maltodextrins or how they are hydrolyzed.

If living yeast is introduced into wort or into a solution of glucose, fermentation starts immediately. Quiescent yeast cells are usually rather more active than the smaller growing ones. Fermentation does not become visible until the solution is saturated with carbon dioxide, and hardly shows on a saccharometer until some gas has escaped, but proof of immediate action is obtained by other means.

The results obtained in experiments with malt wort can be used to explain the action of yeast in other cases.

In the use of yeast for bread-making large amounts are put into the dough, and the fermentative activity is of primary importance. Brewery yeast is unsatisfactory for bread-making, for it is rapidly inactivated at high temperatures ( $35^{\circ}$  C.) by certain yeast poisons in the flour. Such yeast grown in distillers' wort is less sensitive, and can be used by bakers. According to J. L. Baker (1917) un-boiled distillers' wort contains these toxins and the yeast crops from such media consist only of cells which are immune, and therefore of use to the baker. One suspects, however, that the hops in brewery wort play a part in making the yeast sensitive and useless for bread-making on a large scale. This case is of interest for rates of inactivation come into prominence.

Yeast activity takes place under many varied conditions. It is only by referring back to the simple constants of growth and fermentation, and to the factors which influence these constants, that the results can be interpreted and the process understood.

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#### CHLOROPHYL COMPLEXITIES.<sup>1</sup>

BY JOHN URI LLOYD, Pharm.M.,

CINCINNATI, OHIO.

1876. Every one has noticed the gradual change in color which a green leaf undergoes as it arrives at maturity and passes into decay. The green color is mostly caused by a substance named

<sup>1</sup> From *The Eclectic Med. Jour.*, Jan., 1920.

chlorophyl, which is found disseminated more or less throughout the entire vegetable kingdom. Chlorophyl is soluble in both ether and alcohol, but not in water. It is a compound body, according to Mr. Fremy; it consists of a mixture of blue and of yellow organic coloring materials. If the blue preponderates the color of the leaf is dark green, if the yellow is in large amount it is light green. The blue coloring matter is not so permanent as the yellow, it decays quicker, frost destroys it sooner, consequently after our plants reach maturity we observe them gradually fade, pass to yellow and finally turn brown. These successive changes of color depend upon the destruction of the chlorophyl. Those acquainted with the art of mixing paints will understand how nature can produce so great a variety of shades with the two primary colors, blue and yellow. Man unconsciously copies after nature in this respect. Our chrome greens are made by mixing prussian blue and chrome yellow.

Chlorophyl is tasteless, it seems to be inert; at any rate, it can be swallowed in large amount without ill effect. It is found throughout almost all the vegetable organic kingdom. The poisonous powerful narcotic plant and the edible cereal are alike bountifully supplied with this pigment, which with truth may be called nature's own dye, for it has never been produced artificially.

Chlorophyl will not form away from the light; plants which grow in darkness are white. Examples of this fact can be frequently seen in potato sprouts in the cellar, or celery which is covered with soil. Although chlorophyl itself is tasteless and inert, its presence under certain circumstances possesses a deep significance. When celery is green, although it may be young, we know it is likely to prove tough and stringy. Experience has taught us that in this instance the production of chlorophyl is accompanied with the growth of woody fiber; that conditions favoring the production of one, contribute alike to the formation of the other. Chlorophyl, which is visible, advises us in this instance of the almost certain existence of woody fiber, but chlorophyl is in no manner connected with this fiber, and it abounds also in vegetable pulps devoid of fibrous tissue.

Potatoes partly grown upon the surface of the ground, turn green upon the side exposed to the sun's rays; the green coloring matter is chlorophyl. Such potatoes are unfit for food; they are acrid and burn the tongue and throat; yet it is not the chlorophyl which imparts the objectionable properties. The light which pro-

duces the chlorophyl facilitates the formation of other organic substances which impart to the green potato its disagreeable taste. Experience has taught us that potatoes of a green color are not desirable as food; naturally we have associated color with taste until we have grown to believe that the innocent chlorophyl is the cause of the unpalatable green potato.

Although our medicinal plants contain chlorophyl in large amounts, there is in one sense no connection between this green coloring matter and the proximate medicinal agent. The chlorophyl of lobelia, belladonna, hyoscyamus, etc., like that of the potato and celery, is formed under the influence of sunlight, which also favors, in a majority of cases, the production of those substances from which the plant derives the power of exerting upon the animal economy its peculiar action. There is no real connection. Conditions which favor the generation of chlorophyl are favorable to the formation of a majority of the active principles of our plants, from which fact we naturally prejudge, arguing that when a plant has arrived at maturity it should be gathered and cured very carefully, so as to preserve the green color.

1919. *Chlorophyl Complexities Untangled*.—Forty-three years ago (1876) the foregoing, by the present writer, was published in the *Eclectic Medical Journal*. Time and again since that has it been necessary, in correspondence as well as in print, to repeat the substance of that contribution. Physicians, as well as pharmacists, are continually concerned with this chlorophyl problem, the consideration of which is seemingly as important to-day as in times gone by.

To the foregoing the writer would now add that seemingly, in the development of chlorophyl in all plants investigated by himself, other products are with the chlorophyl very intimately associated, this either by adhesion or mechanical combination, all of which in natural setting are colloidal. Chief among these we find certain vegetable waxes, fats and oils, prevailing generally throughout the vegetable kingdom, and seemingly inert therapeutically. Whether they are formed as a needful accompaniment to chlorophyl, or as by-products generated by and with the chlorophyl, is, in the direction of this paper, unimportant. And yet as concerns their presence and their influence on pharmaceutical preparations, they assume importance to a degree but yet imperfectly understood.

Be it said that the utmost difficulty is experienced by whoever attempts, with the ordinary pharmaceutical processes, to untangle these chlorophyl-affiliating combinations. Whatever menstruum dissolves chlorophyl dissolves also these waxes and fats; whatever menstruum precipitates chlorophyl from solution also precipitates the waxes and fats. This can be demonstrated by a single experiment, as follows:

Extract from a chlorophyl-bearing vegetable substance, by means of official alcohol, the soluble content. The percolate, rich in chlorophyl, will be more or less green, in accordance with associated coloring matters. Add to this percolate an excess of water; a green precipitate will form that also varies in shade, in accordance with the associated by-products. It may be deep green, as with blue grass; it may incline to blue, as with freshly tinctured rye leaves when in their bluest condition. It may be soft and oily, as when obtained from *Thuja occidentalis*, or it may be hard and waxy, as obtained from a number of different green vegetable tissues. And yet in it all the dominating fact is that chlorophyl, with the concomitant associates, dissolves in the alcohol and is precipitated by the water. Take these same green plants, percolate them or macerate them in water, cold, warm or boiling. The liquid produced is not green, the chlorophyl being either left in the material or destroyed by the manipulation. Nor are the chlorophyl-bound waxes and fats dissolved by the water—they remain in the drug with the insoluble chlorophyl.

Take the green oily precipitate produced by adding the water to the alcohol solution. It is more or less soluble in chloroform, ether, alcohol and other liquids that dissolve fats, waxes and oils. Upon the contrary, this material refuses to dissolve in glycerine, syrup and watery liquids, the chlorophyl and its associates being hostile to such liquids.

Sum it all up, the chlorophyl problem in the sense presented herein, has been in manipulative pharmacy most perplexing, this by reason of the fact that it not only is of no value in therapeutic directions, but is a mighty disturber.

Comes in now, through what is known as colloidal chemistry, the opening of the door that permits the pharmaceutical manipulator to exclude from preparations all these enemies to good pharmacy. To untangle these complexities, separate from them those of therapeutic value, is now feasible, and by this step upward the profession

of medicine obtains pharmaceutical compounds deemed impossible until came this awakening opportunity.

Comes now the necessity of revising our opinions in many directions where past assertions, most pronounced, were made, regarding materials seemingly understood, such materials, once supposedly insoluble in water, being actually soluble to any degree, provided they are by colloidal processes untangled from plant structural affiliations with chlorophyl and its associated bodies.

### PLATINUM PRODUCTION IN RUSSIA.<sup>1</sup>

CONSUL ALFRED R. THOMSON, Omsk, Siberia, Sept. 9, 1919.

The mining districts of the Ural Mountains in Russia produce more than 90 per cent. of the world's supply of platinum. The following table indicates the composition of the crude platinum deposits in three of these regions, the percentages of pure platinum therein, and the percentages of other metals combined therewith:

Metallic Composition.	Nikolae Pavdinsk Region. Per cent.	Nizhni Tagil Region. Per cent.	Goroblagodat Region. Per cent.
Platinum.....	86.50	75.40	84.50
Rhodium.....	1.15	0.30	2.90
Iridium.....	....	4.30	0.90
Palladium.....	1.10	1.40	0.05
Iridium osmique.....	1.14	0.50	0.70
Osmium.....	....	....	0.03
Chalk.....	0.45	4.00	0.06
Iron.....	8.32	11.50	7.65
Lime.....	....	....	....
Quartz.....	....	1.30	2.10
Gold.....	....	1.30	....
Residue.....	1.34	....	1.08

*Deposits of Platinum—Increase in Platinum Production.*—Crude platinum in the three regions mentioned is usually deposited in layers of sand 3 to 7 feet thick, along the River Isse and its branches,

<sup>1</sup> *Commerce Reports*, Nov. 24, 1919.

the yield varying from a fraction of a dram up to one-half ounce of crude platinum for each ton of sand. Such platinum has the appearance of irregularly formed diminutive grains of a steel-gray color. Because of its highly magnetic properties this form of the mineral is often termed magnetic platinum. Large nuggets of crude platinum are rare, but they have been discovered in weights varying up to 18 pounds.

Crude platinum known as Issovka in the regions named is extracted from the bed of the River Isse and its branches and in the neighboring ravines. Such platinum has the appearance of fine scales of a clear silver color.

Platinum was discovered in the Urals in 1819 but was not utilized until 1825, when the Russian Government began to employ this metal for the coinage of 3-ruble pieces. Up to the year 1845, Russian currency was coined approximately equivalent to \$2,125,000. During the period from 1846 to 1850, the average annual production of platinum did not exceed 180 pounds troy; but from 1880 to 1890, the average annual production was 8,800 pounds. The production for the year 1901 was 17,072 pounds. Refined platinum is usually sold in the form of leaves or wire.

*Government Control of Sale of Platinum.*—Since March, 1919, the Omsk government has controlled the sale of platinum in the territory under its jurisdiction. This control requires that producers of platinum sell the crude metal to the government refining assay office, which paid the producers half of the value of the metal in Russian paper currency, the balance being paid in currency after the sale of the metal by the State Bank. The occupation of the Ural districts by the Soviet government's authorities in July and August, however, limits the Omsk government's control to such supplies of crude platinum as may have been brought within its jurisdiction.

According to estimates made by the government refining assay office at Ekaterinburg last May, the time required to refine a consignment of 440 troy pounds of crude platinum was six weeks, and the cost of the labor in connection therewith was 150,000 rubles. At that time the actual cost of such quantity of crude platinum was 5,000,000 rubles. From such quantity of crude platinum, the average yield of refined platinum was 352 troy pounds, which, valued at the combined cost of the labor of refining and the price

of the crude metal, cost 5,150,000 rubles. Thus 1 troy pound of refined platinum cost 14,630 rubles. The rate of exchange then prevailing being approximately 20 rubles to the dollar, a troy pound of refined platinum may be said to have cost the Omsk Government \$732.

[Prepared by the Russian Division, Bureau of Foreign and Domestic Commerce, Nov. 15, 1919, chiefly from the General Survey of the Principal Branches of the Mining and Metallurgical Industry (in Russian), authorized by the Russian Mining Department.]

Platinum is found in Russia only in the Urals. In recent years platinum has been produced chiefly in the Nizhni Tagil region, on the western slopes of the Ural Mountains, and in the Issov region, on the eastern slopes. The latter is divided into two districts—Goroblagodat and Bisser. Platinum has also been obtained in the northern Urals—in Nikolae Pavdinsk and Rasstess districts and in the mines of the Syssert district. In the Issov region the production is concentrated in the basin of the River Issa. To the north of this region, near the borders of Rasstess and Nikolae Pavdinsk districts, platinum is obtained in the Rivers Sosnovka, Kytlymam and the Little Kosva. Still further north platinum is obtained, together with gold, in the left tributaries of the River Vagran, and in the basins of the Rivers Lobva, Nyasma, Lyalya, Aktai, Emekh, Talitsa, etc.; here platinum is secondary to gold. Platinum is obtained under the same conditions in the Little Sosva River. It is also found east of the above-mentioned regions in beds located in the River Ivdel.

To the south of the Issov region, in the properties of Barantchinsk, Verkhneturinsk and Nizhneturinsk Mills, platinum is dredged in the tributaries of the River Tagil and in the Rivers Imyannyni and Tura, and in the tributaries of the River Salda. In the Nizhni Tagil property there are very rich beds in the valleys of the Rivers Visim, Martyan, Sisim, Tchaush, Tchernaya, etc.

Besides Russia, platinum is also produced in Colombia, Australia and in Oregon and California; but all these do not produce more than 10 per cent. of the world output.

*Production and Exports of Platinum.*—The following figures show the production of platinum in Russia every fifth year, from 1843 to 1898, and annually since 1901:



Years.	Poods <sup>a</sup> .	Years.	Poods <sup>a</sup> .	Years.	Poods. <sup>a</sup>
1843.....	214	1893.....	311	1909.....	313
1848.....	2	1898.....	367	1910.....	335
1853.....	62	1901.....	389	1911.....	352
1858.....	10	1902.....	375	1912.....	337
1863.....	131	1903.....	367	1913.....	299
1868.....	123	1904.....	306	1914.....	298
1873.....	96	1905.....	320	1915 <sup>b</sup> .....	206
1878.....	126	1906.....	353	1916 <sup>b</sup> .....	150
1883.....	216	1907.....	329	1917 <sup>b</sup> .....	187
1888.....	166	1908.....	299	1918 (to July 1) <sup>b</sup> ..	25

<sup>a</sup> 1 pood = 40 funts = 526.64512 troy ounces.

<sup>b</sup> Taken from Izvestya Gornago Otdela for August–September, 1918.

From 1887 to 1913 Russia produced 7,837 poods of platinum and exported 6,428 poods, or 82 per cent. This crude platinum was exported to France, 70.09 per cent.; Germany, 29.13 per cent.; England, 0.78 per cent. About 400 to 450 poods of platinum are used annually, and half of this amount is used in the United States.

The supply of platinum in explored mines is estimated at 7,000 poods. The nuggets found in the Urals were sometimes of considerable weight: In 1827, 10<sup>9</sup>/<sub>16</sub> funts; 1831, 20<sup>7</sup>/<sub>48</sub> funts; 1832, 19<sup>13</sup>/<sub>16</sub> funts; 1843, 23<sup>1</sup>/<sub>2</sub> funts.<sup>1</sup>

## NOTE ON SINGLE CHAMOMILES.<sup>2</sup>

By E. M. HOLMES, F.L.S.

Having recently had samples of single chamomiles sent to me for identification, I was much surprised to find that the flowerheads were not those of *Anthemis nobilis*, but of *Matricaria chamomilla*. As there is no double variety of the latter in commerce, while there are sold in Scotland—or, at least, in Aberdeen—the true wild single flowers of *Anthemis nobilis*, this is all the more curious. On making further inquiries, I found that several wholesale houses in London were in the habit of supplying the flowers of *Matricaria chamomilla* when single chamomiles were ordered; and even in

<sup>1</sup> Taken from Dobrokhotov's "The Urals;" 1 funt = 13.166128 troy ounces.

<sup>2</sup> From *The Pharmaceutical Journal and Pharmacist*.

Edinburgh the same seemed to be the case, although the single flowers of *Anthemis nobilis* are distinguished, by those who know where to get them, as at Aberdeen, as "Scotch" chamomiles.

This confusion may be due to the fact that single chamomiles do not figure in the usual wholesale drug lists. It is, however, possible that those who order single chamomiles may really wish for English double chamomiles in preference to the cheaper French and Belgian double chamomile flowers, since the English have always some of the central florets still remaining tubular and yellow, and these are said to afford more essential oil than the double or ligulate florets. It is noticeable that in "Pharmacographia" (2nd ed., p. 385) it is stated that "such flowers, having a somewhat yellow centre, are called by druggists '*Single Chamomiles*.'" It would be interesting to learn from different parts of Great Britain what the retail trade understand by the name "Single Chamomiles," or what they wish for when ordering "single" chamomiles from their wholesale houses.

It is remarkable that the German chamomile is the kind now official in the U. S. Pharmacopoeia of 1906, in which the Roman chamomile, *Anthemis nobilis*, is conspicuous by its absence. Yet Maisch states that "German chamomile has less agreeable qualities than the English chamomile, but medicinally may be substituted for it." ("National Dispensatory," 1886, p. 966.)

It may be pointed out that *Matricaria chamomilla* has smaller flowers and a hollow, conical receptacle, and no *paleae* or scales below the florets, while *Anthemis nobilis* has *membranous scales* and a solid conical receptacle. The odor of the two is also distinct.

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## GLASS MANUFACTURE AT THE END OF THE WAR.<sup>1</sup>

BY MORRIS W. TRAVERS.

During the war many British glass factories were engaged to a very considerable extent in producing goods and materials which had previously been partly or wholly imported from enemy countries, but which were equally indispensable in war or peace. Plant

<sup>1</sup> Communicated by Section B (Chemistry) of the British Association for the Advancement of Science. Abridged. Reprinted from *The Journal of the Society of Chemical Industry*, Oct. 31, 1919.

and labor were diverted to these special purposes; and some branches of the industry in which the country had already secured a pre-dominant position suffered severely, other branches developed, and entirely new branches of the industry were established. In common with all other industries, the glass trade suffered severely from shortage of labor and material, and particularly owing to the fact that as soon as the lads became sufficiently highly trained to be really useful workmen they were often called up for military service. Furnaces and plant had been worked beyond the economic limit, and were badly in need of repair before the signing of the armistice made it no longer necessary to carry on at all costs. The fact that much of the new constructional work carried out during the war was essentially of an emergency character, carried out with war materials and at war costs, has also to be considered when reviewing the position at the end of the war.

The British glass trade may well be proud of the part which it has played in the war; but there is no little danger that while we continue to celebrate our victories, we may lose the opportunity of consolidating our position. Any scheme devised for the safeguarding of the industry can only be effective if the industry strain every effort to attain to the highest pitch of efficiency; for we may be certain that our late enemies will also strain every effort to win back the positions which they formerly held. They have still their factories, generally in good working order, much of their trained labor and management, and above all a great store of knowledge and experience.

Circumstances arising out of the war have done much to dissipate the idea that success in industry depends upon the possession of trade secrets. The Society of Glass Technology and the new trade associations have already done much to bring manufacturers together, and to promote the spirit of coöperation. Such research as has been carried out during the war has aimed rather at the solution of problems arising out of the need for producing goods previously imported from enemy countries, and it is difficult to lay one's hand on a really original discovery in connection with glass. However, the lines which future investigations must follow are fairly well defined.

The difficulties attending the scientific investigation of glass are extraordinary. We have as yet no knowledge of the nature of glass, and experimental methods have yet to be developed. Glass

is often vaguely referred to as "a super-cooled liquid rather than a solid," and sometimes as a "colloid." Certain opaline and colored glasses certainly contain ultramicroscopic particles; but though there is reason to believe that the complex technical glasses are not simple super-cooled liquids, positive information as to their true character is lacking. Vague speculation in the absence of facts is unprofitable.

The difficulty of investigating the properties of technical glasses is enhanced by the fact that, unless the precautions taken in the manufacture of optical glass are observed, different samples of glass from the same pot may vary materially in composition. Technical glasses often, if not usually, actually represent unstable systems. That it is difficult to find any close relationship between the composition and properties of technical glasses is not, therefore, to be wondered at. At the outbreak of war the independent workers who undertook the investigation of glass must have been struck with the paucity of journal and textbook literature on the subject, and with the fact that such literature as existed contained no practical details and a few analyses. In the case of miners' lamp glasses official tests were established, and the requirements of the makers of lenses, etc., were definitely known. It appeared, however, that few chemists ever tested the glassware they used in their laboratories; the results of a few tests had been published, but as to which of the various brands were really the best was rather a matter of opinion, or even of prejudice, than of scientific proof.

It is generally recognized that, at a comparatively early stage in the war, British manufacturers succeeded in producing glasses for many essential purposes which compared very favorably with the foreign goods, but it will be unfortunate if they fail to realize that there is yet scope for improvement. No resistance glass for chemical glassware has yet been discovered which is sufficiently highly resistant to all ordinary reagents to be considered to be an approach to perfection. It must be admitted that the lamp workers (workers at the table blowpipe) have reason to be highly dissatisfied with the general quality of the tube with which they have had to work. Difficulty of obtaining materials has certainly been a handicap to the manufacturer. However, it is a fact that, while a first-class lamp-working glass must be soft, and must have a low melting point, these glasses "plain" (free themselves from seeds or bubbles) only when very strongly heated in the furnace. The

poor quality of much of the tube manufactured in this country is due to the fact that the furnaces are not capable of working at high enough temperatures.

Almost nothing is known of the chemistry and physics of the founding and plaining of glass, exactly why it is, for instance, that a "checked" pot of metal will not "plain," or how and why the various kinds of cords are formed. We have very little quantitative knowledge of the properties of plastic and liquid glass, and very few attempts have been made to work out methods of investigation. Glass has, of course, no melting point, but perhaps the point of cohesion of two pieces of glass in optical contact, which seems to be quite sharp, may serve as a physical constant. The viscosity of glasses, about which nothing is known, is a matter upon which information would be of use to manufacturers who employ mechanical methods of glass blowing.

There is considerable scope for investigations on the materials used in the glass trade, particularly with a view to substituting cheaper materials for those in use before the war. The best quality of resistance lighting ware manufactured in Austria before the war contained a large proportion of boric acid, which would make the goods almost prohibitively expensive at the present price of borax. A good deal has been done during the war in the way of substituting soda for potash in glasses, but the results, at least so far as glass or electric lamp bulbs and lamp-working tubes are concerned, have not proved satisfactory. However, systematic research may be fruitful of results. The influence of ingredients of glasses, such as magnesia and alumina, which have generally been introduced into glasses accidentally as impurities in the raw materials, is a subject for research.

Prof. Boswell and others have carried out useful investigations on British sources of important glass-making materials, such as sand and feldspar, but the results have not been highly satisfactory, possibly partly owing to circumstances arising out of the war. In 1915 it was still possible to obtain Swedish feldspar containing 13 per cent. of potash and very little iron, delivered flour-ground in London at less than £3 per ton. During the present year the cost of Cornish feldspar, containing 10 per cent. of potash and a considerable amount of iron, delivered in lumps in London, cost over £7 per ton. The difference in the quality of the material is even more important than the increase in price.

Except in some of the larger works, very crude methods are employed in the handling and treatment of materials, and in this the glass trade may be considered to be very backward. The best methods of grinding and mixing batch and cullet, and the use of magnetic separators, conveyors, etc., in the industry really require investigation. The treatment of different kinds of material requires special study. On the proper treatment of the materials and the mixing of the batch depends the quality of the glass, and the saving of loss due to stones and cords. Glass makers are hard on machinery, which they cordially dislike, but which they will have to put up with if the trade is to hold its own against foreign competition.

Regenerative or recuperative glass-fired pot furnaces have for some time been in use in this country, but recent attempts to work them intensively have not met with a great measure of success on account of the repeated failure of the refractory materials in the furnaces and pots. When working at full pressure, and using open pots, it is possible to fill the pots after the blowers have stopped work in the evening, and to found, plain, and cool off the metal by the next morning. Thus it is possible to work the factory with a single shift of blowers working about 48 hours a week. However, to work this single shift the glass must be got ready within the twelve hours.

Continental glass manufacturers have succeeded in working in this way, and for the sole reason that they are provided with superior refractory materials. It appears that satisfactory fire clays exist in this country, and the production from them of suitable fire bricks, siege blocks, pots, etc., should not present insuperable difficulties. The problems await the early attention of the Glass Research Association. The matter is one of vital importance, for the saving of fuel alone is 50 per cent. of that used in the non-regenerative furnaces.

The position with regard to tank furnaces is more satisfactory, but much may be done towards the improvement of the refractories used in their construction. The increase in the cost of fuel and labor also calls for close attention to improvements in gas producers and mechanical accessories.

During the war considerable progress was made in the manufacture of mould-blown goods, such as electric lamp bulbs, and scientific and illuminating hollow ware, which differ from common bottles

in that the goods show no seam, the glass being turned in the mould during the process of blowing. Mould-blown goods cannot be classed as artistic, but from the utilitarian standpoint they are often superior to the hand-made, being consistently true to pattern, and much the cheaper.

Progress in the application of mechanical methods to the production of this class of goods has been made only to the extent of introducing American machines, such as the Empire machine and the Westlake machine, which two British firms have installed for the manufacture of electric lamp bulbs.

Progress in the manufacture of jars, bottles, etc., from glass produced in tanks has been retarded rather than advanced by the war, but manufacturers seem anxious to make up for lost time. It must be admitted that more actual progress is being made in America than in this country, and there is a tendency on the part of our manufacturers rather to purchase the rights to use American machinery than to spend money on the investigation and development of new processes. Enterprise of this kind is very costly, and more than one American invention is credited with having cost those who undertook the development of it more than half a million sterling.

The output of glass tubing has been enormously increased, particularly for uses connected with the war. In many glass houses men engaged in the hand-made trade became tube drawers, and soon became highly skilled at the work. The methods of working employed varied greatly, and it would be interesting to obtain statistical information as to their relative efficiency. It must be allowed that, as much of the tube was drawn in glass houses not specially designed for tube drawing, the men were often at a serious disadvantage. If the output is to be large, a tube shop must be so designed that the men have to walk the minimum distance between the processes of gathering, marvering, reheating, etc. Tubes over one inch in diameter should certainly be annealed before issue, which is not usually done.

Several methods of tube drawing by machinery have recently been patented in America, but little is yet known as to their merits.

Our knowledge of the processes of annealing is not satisfactory, but it has certainly been extended during the war, and in this connection the thanks of the glass trade are due to Mr. F. Twyman, of Messrs. Adam Hilger, Ltd., whose valuable contribution to the study of the subject has been published in the *Journal of the Society*

of Glass Technology. The Hilger instrument for testing goods after annealing has found wide application.

The fact is that both ornamental flint glass and common bottles anneal without difficulty, the one on account of the nature of the glass, the other on account of the fact that the lehrs contain a large mass of hot material, the temperature of which must naturally change slowly. However, in dealing with light articles, particularly when, as in the case of chemical or illuminating hollow ware, resistance glasses are used, considerable difficulties are experienced. The glass is first chilled in the mould so as to set up the condition arrived at in the so-called toughened glass. An unannealed beaker will stand any amount of rough treatment, and liquid may be boiled in it. However, it cannot be *cut off*, and it may at any moment fly to pieces. In such an article the outer surface is probably fairly uniformly in compression and the inner surface in tension.

The first stage in the annealing of such goods is to heat them to a temperature not far below the softening point for a sufficient time to eliminate the stresses. This is the vital part of the process, for it seems as if a badly annealed article were practically even more unstable than such an article before annealing, owing to the inequality of the strains. Very even and regular heating is necessary, and this is only attainable in specially constructed lehrs heated from below as well as from above. The cooling must be at such a rate as to avoid the introduction of fresh strains in the glass. The annealing of light hollow ware is of vital importance.

In branches of the trade in which the goods have to go through a number of processes, success or failure depends very largely upon the proper layout of the works, and the arrangement for transporting the goods so as to avoid breakage in passing from department to department; and very close attention will have to be paid to working conditions, to the comfort of the work people, and to their convenience in the matter of hours of labor. The scientific study of problems relating to industrial administration has made great progress in America, and is now receiving attention in this country.

The foregoing remarks apply to the glass industry in general, but the varied character of the numerous branches makes it quite impossible to deal with matters of detail. At the moment special interest attaches to certain branches of the industry which are scheduled for protection in accordance with the new trade policy. These are: "Optical glass, including lenses, prisms, and like optical de-



vices; scientific glassware; illuminating glassware." The country is now practically self-supporting with regard to scientific hollow ware, and it may be hoped that the labors of the Standardization Committee of the Society of Chemical Industry, which have aimed at the standardization of chemical apparatus, may have been of value to the industry. The output of lamp-blown apparatus and of graduated apparatus has increased enormously, but it may be anticipated that this branch of the industry will meet with keen competition. The scientific public, critical of home-made goods, has suddenly awakened to the fact that much of the imported graduated ware was very inaccurate, and is insisting on a higher quality of goods, which the British manufacturers are succeeding in supplying.

Though great progress has been made in the manufacture of illuminating glassware, neither plant nor labor has been sufficient to cope with the demand. Optical glass was manufactured in this country before the war, but on a scale totally insufficient to meet our requirements, and during the past five years the development of the industry has been extraordinary. It must be remembered that while a very inferior lamp chimney will still serve a very useful purpose, optical glass must be good, indeed, very good, or it will be quite useless.

In this part of the industry refractories play an important part, for if the pots will not withstand the solvent action of the glass, as the pot material dissolves it changes its composition, and also gives rise to stones and cords. The iron oxide from the clay tends to discolor the glass, and the color cannot be corrected by the use of manganese or other reagents. Stirring the molten glass, which is necessary in order to make it homogeneous, naturally presents difficulties which have been only partially overcome. The reduction of the wastage between the founding of the glass and the formation of the blocks and blanks supplied to the lens maker offers scope for investigation. Though much research work has already been carried out in this country and also in America, where the industry is also a new one, much remains to be done. Very high credit attaches to the work already accomplished.

Finally, while we must try and hold on to what we have won, we must endeavor to win back what we have lost. The diversion of plant and labor previously engaged in the manufacture of high-class ornamental glassware has resulted in the disorganization of

a branch of the industry in which the country held a predominant position. It must be remembered that the Central Empires formed one of our best markets for this class of goods.

The replacement of hand-made articles by machine-made goods is perhaps one of the unavoidable consequences of civilization, and, balancing the advantages and disadvantages, we may, on the whole, gain by the change. While the machine may increase the perfection of the form of the article, though perfection of form may not imply enhancement of beauty, the material almost always suffers in mechanical treatment. There is a play of the lights on the surface of a piece of hand-worked English flint glass which is never to be found in a mould-blown article. American mechanical reproduction, of English cut glass are very wonderful, but they absolutely lack the craftsman's touch.

The branch of the trade should remain largely a handicraft. Economies can, however, be introduced in many directions, and there is no reason why the old-fashioned round furnace should still be used. Such fuel-wasting machines should, in the national interest, be prohibited under D. O. R. A., or her successor.

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## METHYL OR WOOD ALCOHOL AND ITS END-PRODUCTS IN THE BODY.<sup>1</sup>

The menace of methyl alcohol or wood spirits to human health, though long known to physicians, has never been adequately appreciated by the public. Heretofore the dangers arising from its introduction into the body have for the most part been confined to some accidental or casual intake of the substance, and larger numbers of fatalities have arisen only in unusual circumstances, such as the criminal adulteration of alcoholic beverages with wood alcohol. With the enforcement of national prohibition, however, the prospect of more frequent instances of harm through the use of this intoxicant in place of the forbidden grain spirits and other drinks containing ordinary ethyl alcohol is unfortunately before the nation. Within the last few weeks the newspapers have been reporting the deaths of more than a hundred persons from the adulteration of alcoholic beverages with methyl alcohol. It therefore

<sup>1</sup> From *Jour. Amer. Med. Assoc.*, Jan. 3, 1920.

becomes more necessary than ever to understand the toxicology of methyl alcohol and its behavior in the body. To combat an enemy we must learn to know its mode of attack.

Chemically, the difference between methyl alcohol ( $\text{CH}_3\text{OH}$ ) and ethyl alcohol ( $\text{CH}_3\text{CH}_2\text{OH}$ ) is not striking, though the methods of preparation are dissimilar. When wood is subjected to destructive distillation, methyl alcohol is one of the products formed. Ethyl alcohol is derived from the fermentation of grains or fruits. Wood alcohol, about 10 per cent., may be added to ethyl alcohol to render the latter unfit for beverage purposes, and the government has ruled recently that such denatured alcohol must bear on the label a special warning concerning the dangers of methyl alcohol. Elsewhere in this issue appears the report of a case of wood alcohol poisoning thoroughly studied with reference to the symptomatology and pathology.<sup>2</sup> When death occurs, there is usually coma, with death from respiratory paralysis. According to our present knowledge, methyl alcohol is eliminated slowly from the body, an end-product of the oxidation in the body being formic acid.

Formic acid,  $\text{HCOOH}$ , has been recognized as an excretory product of methyl alcohol since Pohl<sup>3</sup> demonstrated, in 1895, that introduction of this alcohol into the stomach leads to an increased output of formic acid in the urine. Hence the latter affords a possible means of ascertaining whether or not wood alcohol has been taken into the organism. A mere qualitative test for formic acid, however, will not suffice; for this substance has been known, at least since 1877,<sup>4</sup> as a normal constituent of the urine. Therefore it is essential to know something regarding the extent to which formic acid may occur in the urine under what may be called normal conditions of living. According to Autenrieth,<sup>5</sup> the quantity eliminated may vary considerably in different persons, though it tends to exhibit a uniformity in an individual living on a fairly uniform diet. The figures approximate 0.25 Gm. a day as an illustrative average.

When methyl alcohol is ingested, the output of formic acid in

<sup>2</sup> Harrop, G. A., Jr., and Benedict, E. M.: "Acute Methyl Alcohol Poisoning Associated with Acidosis," *J. A. M. A.*, Jan. 3, 1920, p. 25.

<sup>3</sup> Pohl, J., *Arch. f. Exper. Path. u. Pharmacol.*, 31: 286, 1895.

<sup>4</sup> Thudichum, *Arch. f. d. ges. Physiol.*, 15: 129, 1877.

<sup>5</sup> Autenrieth, W.: "Ueber den Ameisensauregehalt des Harns, normalerweise und nach Eingabe verschiedener Substanzen, München." *Med. Wehnschr.*, Aug. 1, 1919, No. 31, p. 862.

the urine promptly increases. For example, a person who had taken 80 Gm. of pure methyl alcohol in the course of eight days showed an extra elimination of formic acid above his usual output equivalent to 5 per cent. or more of the consumed spirits. It will be observed that even when these relatively innocuous doses were taken, a quantitative investigation betrayed the intake. With larger doses, methyl alcohol itself, which is missed in such instances as that just cited, may appear in the urine. Other alleged precursors of formic acid, such as glucose, and lactic acid which might readily be taken into the body in exceptionally large quantities in the course of an ordinary regimen, were found by Autenrieth to be without appreciable influence on the output. Formaldehyde,  $\text{HCOH}$ , did not produce an increment; but formic acid itself was quite resistant to oxidation in the body, so that unlike many other organic acids it again reappeared in the urine in considerable proportions unchanged. Fortified with these facts, the chemist will be better prepared to ascertain the occurrence of poisoning with wood alcohol when the direct evidence may be lacking or inconclusive. At the present juncture the public should be made to appreciate that methyl alcohol is a dangerous poison; that one of its serious effects is permanent blindness, and that it may be so prepared as to be ordinarily indistinguishable by odor or taste from ethyl alcohol. It should be emphasized that the selling or promoting the sale of or use of either methyl or ethyl alcohol as a beverage is the doing of an unlawful act.

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#### FIXATION OF PRICES NO NEW THING.<sup>1</sup>

Mr. L. Zions, Secretary of the P. A. T. A. of New South Wales, sends us the following extract from a magazine in his library. It is particularly apposite at the present time, in view of the world-wide endeavor to reduce prices through the instrumentality of government regulations.

The article was written by the late Elbert Hubbard, and appeared in the American *Era* magazine of April, 1914. Mr. Hubbard had just been reading a book, entitled "The Common People of Ancient Rome," by Professor F. F. Abbott. In his own inimitable style he reviews the book under the title of

<sup>1</sup> From *The Australian Journal of Pharmacy*, Nov. 20, 1919.

### THE DIOCLETIAN EDICTS.

"I have just been reading a most interesting book, entitled 'The Common People of Ancient Rome,' by Frank Frost Abbott, Kennedy, Professor of Latin Language and Literature in Princeton University.

"As long as the common people of Rome were in the ascendant, Rome ruled the world. When they became pauperized through paternalism, weakness, degeneration, disease and dissolution were at the door.

"I recommend very few books—beside my own—but this book by Professor Abbot on the common people of Rome should be read by all of the common people of America.

"There is one chapter especially that is worth the price of admission, and that is the chapter on the Emperor Diocletian, who lived in the fourth century after Christ. This man had a deal to do with ushering in the dark ages. His intent and desires were right, but he had a wonderful itch for butting in and taking charge of everything. The people were not allowed either to choose their own religion or to do business in their own way. Diocletian knew nothing about natural law; that is, spiritual law.

"High prices then prevailed. Diocletian devised a scheme for keeping them down—this, in the interests of the common people, for politicians, propagandists, reformers, rulers, who live off the common people, have ever been anxious to show the common people what to do. So comes Diocletian, solicitous on account of high prices. He sends his secretaries through the market places, makes a list of seven hundred commodities, and the secretaries fix maximum prices at which things should be sold. The penalty for charging more than the established price was death.

"In order that there could be no misunderstanding, Diocletian had the names of the articles and the prices above which they should not be sold cut in stone and placed on the walls all around the markets.

"What was the result? Simply this, that the common people who had been busy producing all of the commodities that ministered to human life became panic-stricken. Animation flagged. Inspiration died. Laughter ceased. No such thing as joyous labor longer existed.

"The threat hanging over them of what the Government proposed to do killed spontaneity, and creation, development and production died.

"And behold, there came the dark ages, when for a thousand years night prevailed; when for a thousand years the world did not produce a poet, an orator, an inventor, an artist, a navigator, a mathematician; when fear was supreme, and hope stood far away in the shadow, shivering and cold, a finger to her lips.

"Our friends in Washington should read this book on the common people of Rome, and learn the lesson, which is: the less rulers mix in, dictate and try to regulate economic activities, the better it is for the common people.

"Well did Thomas Jefferson say, 'That Country is governed best that is governed least.'"

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## CORRESPONDENCE.

### PHARMACOPOEIAL CONVENTION, MAY 11, 1920

#### SECOND NOTICE.

In harmony with the requirements of the By-Laws, attention of interested parties is called to the meeting of the Tenth Decennial Pharmacopoeial Convention of the United States, to be held beginning at 10.00 A.M., May 11, 1920, at the Willard Hotel, Washington, D. C. All incorporated bodies and other institutions entitled to membership in this Convention are entitled to at once apply to Dr. Noble P. Barnes, Arlington Hotel, Washington, D. C., for the necessary blanks for membership in the Convention.

Prior to the meeting of the Convention, the Committee on Credentials will meet in Washington to consider all applications which are made. It is important, therefore, that all applications for membership should be in the hands of Dr. Barnes at least six weeks before the date of the meeting. It will be difficult to consider, properly, credentials which are delayed beyond that date and especially those which may be presented at the time of meeting.

Sincerely,

H. W. WILEY, President, 9th Decennial  
Pharmacopoeial Convention of the  
United States.

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## UNITED STATES PHARMACOPOEIAL CONVENTION.

### PROPOSED AMENDMENTS TO CONSTITUTION AND BY-LAWS.

The following amendments to the Constitution and By-Laws are recommended by the Board of Trustees for adoption by the Convention at Washington, May 11, 1920.

Words to be deleted are enclosed in brackets and words to be added are printed in italics:

### CONSTITUTION.

#### ARTICLE II.

#### MEMBERSHIP.

SECTION 1. The members of the United States Pharmacopoeial Convention, in addition to the incorporators and their associates, shall be delegates elected by the following organizations in the manner they shall respectively provide: Incorporated Medical Colleges and Medical Schools connected with Incorporated Colleges and Universities, Incorporated Colleges of Pharmacy, and Pharmaceutical Schools connected with Incorporated Universities, Incorporated State Medical Associations; Incorporated State Pharmaceutical Associations, the American Medical Association, the American Pharmaceutical Association [and] the American Chemical Society, *the National Association of Retail Druggists, and the National Association of Boards of Pharmacy*; provided that no such organization shall be entitled to representation unless it shall have been incorporated within and shall have been in continuous operation in the United States for at least five years before the time fixed for the decennial meeting of this corporation.

SECTION 2. Delegates appointed by the Surgeon-General of the United States Army, the Surgeon-General of the United States Navy, and the Surgeon-General of the United States Marine-Hospital Service, the Secretary of Agriculture, the Secretary of Commerce and Labor, the Association of Official Agricultural Chemists, the Association of State and National Food and Dairy Departments, the National Wholesale Druggists' Association [and] the National Dental Association, *the American Drug Manufacturers' Association, the United States Division of Customs, and the University of Havana*, and by the organizations not herein before named which were admitted to representation in the Convention of 1900, shall also be

members of the corporation. Each body and each branch of the United States Government above mentioned shall be entitled to send three delegates to the meetings of this corporation. But no such delegates as are provided for in this article shall be members until their credentials shall have been examined and acted upon as provided for by the By-Laws. Delegates admitted as members at any decennial meeting shall continue to be members of the United States Pharmacopoeial Convention until their successors shall have been appointed and admitted as delegates to the ensuing Convention and no longer.

#### ARTICLE V.

##### MEETINGS.

The regular meetings of this corporation shall be held once in ten years. The time of holding the decennial meeting shall be upon the second Tuesday in May, in the first year in each decade ending in zero, and the place of meeting shall be in the City of Washington, D. C. *Unless in case of emergency, the Board of Trustees and officers of the Convention, by joint vote shall select some other place of meeting and some date within the same year other than the second Tuesday in May.* The first decennial meeting shall be held in the year 1910.

#### ARTICLE VI.

##### AMENDMENTS.

Every proposition to alter or amend this Constitution shall be submitted in writing to the Board of Trustees, and having received the votes of at least five members of the Board of Trustees, shall be [published in the medical and pharmaceutical journals] *submitted to the medical and pharmaceutical press*, at least three months before the decennial meeting of the United States Pharmacopoeial Convention, when, upon receiving the votes of at least three-fourths of the members present and voting, it shall become a part of this Constitution.

##### BY-LAWS.

#### CHAPTER III.

##### OF THE TREASURER.

ARTICLE II. He shall pay no moneys except on the written order of the Board of Trustees. All bills must be accompanied by proper



vouchers and all payments shall be by checks, and such checks drawn by the [Treasurer] *Secretary of the Board of Trustees* for the payment of moneys shall be *signed by the Treasurer and countersigned* by the Chairman of the Board of Trustees to become valid.

#### CHAPTER IV.

##### OF THE TRUSTEES.

ARTICLE V. There shall be an annual meeting of the Board of Trustees *at such time and place as the Board shall direct*, unless in any year such meeting shall have been declared unnecessary by a special vote of the Board. For the taking of such vote and for other matters the Board shall have the right to transact business by correspondence. Special meetings of the Board of Trustees shall be called upon the written request of at least three members, and the Chairman shall have the power to call a special meeting whenever he shall deem it necessary. The members of the Board of Trustees shall receive no compensation for their services, but traveling and other necessary expenses which may be incurred by them shall be paid from the funds of the Convention.

#### CHAPTER IX.

##### OF MEETINGS.

ARTICLE II. The order of business at the first session of each decennial meeting shall be as follows:

*Section 4. Report of the Chairman of the Board of Trustees, the Secretary of the Board of Trustees and the Treasurer of the Convention.*

Change the present Section 4 to Section 5, Section 5 to 6, and 6 to 7.

JAS. H. BEAL, *Chairman.*

H. M. WHELPLEY, *Secretary*

January 30, 1920.

Board of Trustees.

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#### ANNOUNCEMENT OF A. PH. A. SECTION ON PRACTICAL PHARMACY AND DISPENSING.

Editor, AMERICAN JOURNAL OF PHARMACY,  
Philadelphia, Pa.

DEAR SIR: As Chairman of the Section on Practical Pharmacy and Dispensing of the A. Ph. A., I am sending out an invitation

and urgent request to all who are interested in the practical work in the store to present papers before this Section next May.

Because of the meeting coming so much earlier than usual, it will be necessary to have the titles of papers furnished me not later than the middle of March and it is desirable that the papers be received at the same time or as soon after as possible.

Some subjects which have been suggested are:

1. Constructive criticisms of the U. S. P. This is particularly pertinent as the U. S. P. Convention follows the next week.

2. The part which the pharmacist is to play in the revision of the U. S. P.

3. Consideration of new remedies.

4. Papers dealing with prescription work.

5. The pharmacist as a clinical chemist. Papers from those who have had experience along this line are especially desired.

6. What professional work can the pharmacist do to take place of that which is passing into the hands of the large manufacturer?

7. A discussion of the affiliation of the drug clerk organization with labor unions and drug clerk strikes.

8. Is it desirable to have laws regulating the hours which the pharmacist may work?

Papers bearing on any phase of Practical Pharmacy will be very acceptable.

Yours truly,

E. A. RUDDIMAN, *Chairman.*

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THE ESTABLISHMENT OF A FELLOWSHIP TO EXTEND  
INDUSTRIAL USE OF GLYCERIN IN THE MELLON  
INSTITUTE OF INDUSTRIAL RESEARCH.

Pittsburgh, Pa.

Jan. 6, 1920.

AMERICAN JOURNAL OF PHARMACY,

145 N. Tenth St., Philadelphia, Pa.

DEAR SIR: A prominent manufacturer has recently established an Industrial Fellowship in this Institution for the purpose of extending the industrial uses of glycerin. The writer, who is the incumbent of the Fellowship, has planned primarily to center the investigation on the substitution of glycerin in place of alcohol for

preservative and extractive purposes in pharmaceutical and allied fields. As you doubtless know, some of the leading authorities have advocated this procedure as being satisfactory in many instances, but it has not so far received critical study.

The Mellon Institute is an endowed institution devoted to scientific research and its application to the industries. The glycerin Fellowship will be conducted in the same manner as all fellowships in operation at this Institute, and as such is not affected by any financial consideration. The data thus obtained by this organization is therefore unique, insofar that it represents the result of research work conducted in an impersonal manner, and is not subject to any private interest. For your guidance, I am submitting a copy of Director R. F. Bacon's last annual report.

I hope that the work will progress in the laboratory, so that a preliminary report of the research may be submitted to you in the near future. Your suggestions and ideas concerning this problem would be highly appreciated, and I would also feel grateful to you if you would give this matter publicity by using the enclosed note in the next issue of your periodical.

Very truly yours,  
MELVIN DEGROOTE.

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## OBITUARY.

### SIR THOMAS RICHARD FRASER, M.D.

On January 4, in the City of Edinburgh, terminated the life of Sir Thomas Richard Fraser, M.D., LL.D., F.R.S., at the age of seventy-eight years. At the time of his decease he was Emeritus Professor of Materia Medica in the Edinburgh University. He was long recognized as one of Great Britain's most eminent physicians and pharmacologists. He was graduated in medicine from this same University in 1862 and in 1872 was appointed a lecturer on Materia Medica, in which branch he early specialized. In 1877 he was elected as Professor of Materia Medica to succeed Sir Robert Christison. He continued in this chair until 1918 when failing health, due largely to a physical breakdown and an accident by which he sustained a fractured leg, compelled his retirement as Emeritus Professor.

He held many positions of prominence in his profession, having been president of the Royal College of Physicians of Edinburgh and was a member of the medical committee appointed to prepare the latest revision of the British Pharmacopoeia. He was a member of the commission to investigate plague and in that connection visited India in 1898. In 1902 he was knighted. He was an honorary member of the Pharmaceutical Society of Great Britain.

Sir Thomas Fraser's scientific standing was based upon his original investigations and his contributions to medical knowledge was mainly along the line of the pharmacologic study of potent remedies. His study of the physiologic action of strophanthus stands out yet as one of the most valuable contributions to the knowledge of that drug and placed it permanently among the valuable heart tonics. As other investigations may be mentioned those of physostigmin and certain snake venoms.

G. M. B.

#### DR. HORATIO C. WOOD.

The demise of Dr. Horatio C. Wood, on January 3, 1920, the widely known authority on therapeutics, deserves more than passing tribute. Although a semi-invalid since 1906, at which time he retired from practice, his researches upon the physiological action of drugs have left a deep and permanent impression upon American medical practice; so much so that he has been called "The Father of American Therapeutics."

Dr. Wood was a man of unusual breadth of vision and a tireless, versatile worker. He was a botanist, pharmacognocist, physiologist, pharmacodynamist, neurologist and clinician; possessed of keen powers of observation and close reasoning, his studies upon the action of drugs upon animals and human beings have become classic, and with Dr. Roberts Bartholow and others he drew international attention to the research work of American therapeutists. He was among the first to differentiate between the empirical use of drugs and the rational use, based on physiological action as determined by animal experimentation. With his classic studies on pharmacology, he ever kept a firm faith in the preëminent value of drugs for the treatment of disease when rightly used, and was ever sympathetic to the claims of pharmacy for recognition as a sister profession.

He was chairman of the U. S. Pharmacopoeial Convention for 1890 and for 1900 and probably was only prevented from continuing as chairman of the convention for 1910 by reason of his illness.

The profession of pharmacy, as well as that of medicine, is greatly indebted to the work of Dr. Wood and pharmacy may well honor him.

As Dr. S. Solis Cohen has written:

"Horatio C. Wood was a giant of soul no less than of intellect. His great influence for good upon the development of American medicine was not confined to his epoch-making contributions in the field of therapeutics, but extended into personal relations as well, and was owing no less to his character as a man than to his preëminence as a scientist. As author and teacher, he will be missed; as a man, he will be mourned."

J. W. E.

### C. CARROLL MEYER.

C. Carroll Meyer passed peacefully away Monday evening, December 15, 1919, after having been unconscious for three days following a stroke of paralysis which, possibly, had been induced by the effects of a murderous assault made upon him about two years ago by a desperate character who has never been apprehended.

"Carroll," as he was familiarly known to his many friends, was born in Philadelphia, November 24, 1854, and, as a boy, attended Saint Joseph's College, 4th Street and Willing's Alley. About July 1, 1869, he was apprenticed to Thomas J. Husband, Third and Spruce Streets, the originator of Husband's Magnesia. He remained there until 1879 when he embarked in business for himself at 1802 Callowhill Street, later removing to 1800 Callowhill Street, and finally, about twenty years ago, to 341 No. 18th St., where he continued the practice of his profession until stricken with the illness which terminated fatally.

The funeral was held Friday, December 19, with services at his late home at 8.30 A.M., followed by public services at 10.30 in the Cathedral of Saints Peter and Paul, with subsequent interment in Cathedral Cemetery. He is survived by his wife and an adopted daughter.

C. Carroll Meyer's connection with the Philadelphia College of Pharmacy dates from the day he matriculated as a student in the

fall of 1871. In the spring of 1872, after the regular winter term had closed, he joined a summer class which met at the College one afternoon each week for study, quiz., etc., under the guidance of the lamented Dean Remington, then assistant to Professor William Procter. He was energetic and studious and became a force for good to his fellow students during the winter term of 1872-3, when he served as one of three lieutenants or assistants to the president of his class, then the Senior Class.

He was graduated March 18, 1873, with the degree of Ph.G., the subject of his graduation thesis being "Ichthyocolloids." He immediately joined the Alumni Association and faithfully served it, as private and officer, during more than forty-six years. He held every elective office except that of recording secretary. He was first elected a member of the Board of Directors in 1883, was president in 1892-3, and served continuously as treasurer from 1900 until his activities were terminated by the Grim Reaper.

He was elected to *active* membership in the College in 1887 and became a *life* member in 1912. He served as a member of the Board of Trustees from 1897 until 1914 when he declined nomination for re-election.

"Love and Loyalty" might well have been his life motto, as these represent his attitude toward the College, his Alma Mater, the Alumni Association, his co-workers, his church and his fellowman, whose servant he ever strived to be.

F. X. M.

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## CURRENT LITERATURE

### MEDICAL AND PHARMACEUTICAL NOTES.

**PICRIC ACID AS DISINFECTANT.**—The use of 5 per cent. picric acid solution is advocated by Cassegrain as a preoperative disinfectant, because it thoroughly disinfects and can be used with soap and water; it does not irritate the skin, and it is approximately 40 per cent. cheaper than iodine. (*New Orleans Med. and Surg. Jour.*; through *J. Amer. Med. Assoc.*, January 24, 1920.)

**INFLUENCE OF URANIUM ON THE BLOOD.**—Mas Magro reports the results of extensive experimental research on the action of uranium on the blood-producing organs. A subcutaneous intraperitoneal injection of a 2 per cent. solution of uranium acetate in rabbits and guinea-pigs caused an epithelial nephritis with death

the sixth or seventh day. This is the effect of the minimal lethal dose. When death occurs in three hours and a half, the blood shows coagulation, thrombosis, precipitation and agglutination. Uranium thus does not induce death directly. (*Plus-Ultra*, Madrid, August, 1919; through *J. Amer. Med. Assoc.*, January 31, 1920.)

CLINICAL IMPORTANCE OF THE COLLOIDAL GOLD REACTION.—The main difficulty with the colloidal gold reaction, Eicke finds, is the preparation of the colloidal gold. The trouble lies in the extreme sensitiveness of colloidal gold to chemical influences; even the alkalinity of the glass may give the solution a bluish tinge and render it useless from the start. Another frequent cause of failure is that fresh, doubly distilled water is not used. The colloidal gold reaction furnishes an interesting proof of the baneful effect of exceedingly slight impurities in water. The main value of the colloidal gold reaction is that it gives us a means for the early diagnosis of neuro-syphilis. At the Rudolph Virchow Hospital, Berlin, it has established the syphilitic origin in many obscure cases. In one case of optic neuritis, the etiology was baffling. The personal and family history was negative. The blood Wassermann test was negative, but the colloidal gold reaction gave the typical curve of cerebrospinal syphilis. The patient, who was seriously ill, was at once given specific treatment with good results. If it should prove possible to simplify the preparation of the colloidal gold, this reaction might be regarded as ideal and would be of the greatest value to medicine. (*Münchener Medizinische Wochenschrift*, Munich, Sept. 12, 1919; through *J. Amer. Med. Assoc.*, January 31, 1920.)

PHARMACOLOGICAL ACTION OF CADMIUM.—Cadmium is a powerful emetic. Parenteral administration of the chloride produces nephritis, and coagulation of protein and necrosis occur at the site of subcutaneous injection. The lethal intravenous dose for cats, rats, and rabbits is low, 2 to 3.5 Mgm. of the metal given as chloride. (Alsberg and Schwartz, *J. Pharm. Exp. Therap.*, 13: 504, 1919.)

J. F. C.

PHARMACOLOGY OF BENZALDEHYDE.—Benzaldehyde relaxes the tonus and inhibits the contraction of isolated smooth-muscle organs. It has a sedative effect on various organs *in situ*. It possesses definite and marked local anesthetic properties, anesthetizing the sensory nerve ending of the frog's skin, of the cornea and of human mucous membranes. Benzaldehyde solutions paralyze nerve conduction. It is very little toxic. (D. I. Macht, *J. Pharm. Exp. Therap.*, 13: 508, 1919.)

J. F. C.

BENZYLALCOHOL.—Injections into the thoracic region of the spinal cord are followed by a severe fall in blood pressure and decreased respiratory movements. It also produces spinal anesthesia. (Voegtlin and Livingston, *J. Pharm. Exp. Therap.*, 13: 513, 1919.)  
J. F. C.

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## SPONGE GATHERING IN TUNISIAN WATERS.<sup>1</sup>

BY CONSUL HARRIS N. COOKINGHAM,

TUNIS, NOV. 11, 1919.

Although the Greek divers have abandoned the sponge fisheries of the Tunisian coast for those of Tripolitan waters, unexploited since the Turko-Italian War, where, it is reported, unexcelled sponges have recently been taken (for the English market, which is paying almost 80 francs a kilo for the best specimens), the sponge beds along the Regency's coast are bringing no small profit to the Sicilian dragnets and harpoonists now plying in the Gulf of Gabes and around the Kerkenna Islands. Sfax, the chief port of southern Tunisia, is naturally the trade center of the industry, the sponge market of Tunisia whence domestic and export prices are regulated. It is interesting to note that for the fine sponges which the Kerkenna fishers obtain the Sfax prices are from 32 francs per kilo (2.2 pounds); sponges from the Gulf of Gabes, of ordinary quality, bring 27 francs a kilo (formerly from 12 to 14 francs). The harpoonists are bringing in good sponges, poorly dried and cleaned, which are sold at 32 francs a kilo in Sfax. There the extremely fine Kerkenna sponges are expected within a fortnight, for sale, it is already announced, at about 50 francs a kilo; these are sold without any preparation whatever to buyers, who themselves clean the delicate tissues.

<sup>1</sup> From *Commerce Reports*, December 31, 1919.

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# THE AMERICAN JOURNAL OF PHARMACY

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MARCH, 1920

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## EDITORIAL.

### THE RESPONSIBILITY OF PHARMACY UNDER PROHIBITION ENFORCEMENT.

The various acts of national legislation leading up to the enactment of prohibition as well as the prohibition enforcement act, have all recognized the use of distilled spirits and wines as medicines. The Volstead Act, more distinctly than its predecessors, takes cognizance of such legitimate use of alcoholic liquors, and attempts to provide the procedure by which the needs of the public for such as medicine can be supplied.

We have reason to believe that in the drafting of this portion of that act careful consideration was given to this subject as one that under the existing knowledge and status of the practice of medicine must be provided for as a public necessity. In the exercise of its law-making prerogative, Congress very properly determined that the use of distilled spirits and wines as medicines must be provided for but that the prescribing and dispensing must be done through the proper channels of professional medical practice and that protective measures must likewise be adopted to restrict the dispensing of these to bona fide prescriptions.

We believe that the Volstead act is the first law enacted by the Congress of the United States that clearly recognizes that pharmacy is a distinct branch of medicine; that its function is to dispense all medicines and that dispensing, even of alcoholic liquors, can be controlled through the profession of pharmacy. This is a principle for which pharmacists have been contending for a long time and the importance of its establishment in the jurisprudence cannot now be fully estimated.

President LaWall, in his presidential address before the American Pharmaceutical Association, considered that this was to be viewed.

as an evidence of confidence in the profession of pharmacy and likewise expressed his opinion that as a whole pharmacy would measure up to this added responsibility. It is evident from the discussions appearing in the pharmaceutical press that many of those engaged in the drug trade entertain different views, and what is even more apparent is the lack of careful reading and digestion of the law and the regulations covering these features of its enforcement.

The fear that any number of "weak brothers" in pharmacy will see an opportunity of reaping "easy money" by infracting this law and by their misdeeds discrediting the entire profession, seems to be one of the stock arguments. The regulations provided for the protection against such violations are certainly stringent, and foolish indeed will be the druggist who engages in "booze selling." He may be assured that sooner or later his transgressions will be discovered and the merited punishment meted out. The penalties are by no means light and both medicine and pharmacy should purge their professions of the violators of anti-liquor and anti-dope laws. In our opinion the dispensing of all medicines that are abused or habit-forming must be restricted to the legitimate medical professions, each functioning within its own proper field of service. This is evidently the intent of the enforcement act as it relates to the use of liquors as medicines, and as its full force and effect become established, the infractions must become notably less and the "weak brothers" either will not appear or will have disappeared.

We share fully the opposition of the pharmacists to being classified as retail liquor dealers. The classification never was appropriate to those engaged in the vocation of the apothecary and now that dealing in beverage alcoholic liquors is outlawed, we hope forever, the necessity for the Treasury Department maintaining the "R. L. D." class has certainly ceased to exist. Pharmacy should congratulate itself and the lawmakers that in the enforcement act "pharmacist" is the term used and that professional title is used to designate the class alone upon whom the responsibility for the proper dispensing of such medicines is placed. The pharmacists are entirely right in demanding that the odium of the retail liquor dealer should not fall upon them in the discharge of what the law now makes a part of their professional duty.

It appears that in maintaining the classification of "R. L. D." the Treasury Department is carrying out the laws now on the statute books, and that to relieve the pharmacists of this objectionable

classification and tax, remedial legislation will have to be enacted. In directing attention to this needed legislation, to correct what is an error on the part of the Government, we do so because of the importance of its bearing at this time. Many self-respecting pharmacists are deterred from dispensing bona fide prescriptions for alcohol or alcoholic liquors because of their objection to taking out the permits and qualifying as now required, and to being classified as Retail Liquor Dealers. As a result, in many sections of the country, physicians are having trouble in having these prescriptions dispensed and the pharmacists are being severely criticized for failing to discharge their duty to the public.

Presumably the pharmacists of the United States want the law modified so that they will no longer have to bear the odium of being liquor dealers. This can only be accomplished by a determined effort that will convince the members of Congress of the real facts. We believe that this object can be attained by a united effort of the drug trade interests and are prepared to lend our utmost efforts in that direction. In the meantime, will pharmacists gain either prestige or public endorsement of this proposition by shirking a responsibility that Congress has already imposed?

The decision as to what is or is not a medicine does not primarily rest upon the pharmacist. The physician has the responsibility of diagnosing and of prescribing whatever remedies he deems are appropriate. Upon the pharmacist devolves the duty of properly compounding and dispensing whatever the physician in his judgment may determine is the medicine required. In the discharge of such professional duty, the pharmacist is not concerned whether this judgment dictates doses of a toxic or a narcotic, an alcoholic remedy or even a placebo. With equal grace and skill and without diminishing in the least his professional spirit, he can dispense any of these or other medicines. The hue and cry against bona fide dispensing of stimulants, in the opinion of the writer, is not justified by any code of professional ethics. The countenancing of any dispensing that is not bona fide, either alcoholic, narcotic or for any other improper motive or use, is beyond the pale of professionalism and should be outlawed, and a pharmacist has at all times the right to refuse to sell or dispense any or all medicines that he either knows or suspects are not to be applied to legitimate practice.

The suggestion has been made by pharmacists in several sections of the country that the government should establish dispensaries

for the dispensing of prescriptions calling for liquors. No provision has been made in the law for any such procedure, and the Internal Revenue Department would not be justified in establishing such a method of dispensing until so directed by Congressional enactment.

It is exceedingly doubtful if government dispensaries would be either a practicable or an efficient means of protecting against the illicit use of such spirits.

The shirking of the responsibility placed upon pharmacy by this Congressional enactment is not without the possibility of working to the detriment of pharmacy. If pharmacists refuse to accept the responsibility placed upon them by the government to dispense distilled spirits and wines *for medicinal purposes*, and insist that prescriptions for such must be compounded only in government dispensaries, the public and legislative bodies may construe this as an indication that the pharmacists are not discharging their professional duties. If such a procedure were to be adopted regarding the dispensing of alcoholic stimulants, it might be considered as a precedent for the same course regarding narcotic drugs or toxic remedial agents, and the profession of pharmacy certainly would be destroyed if such a procedure was to be carried out to its possible conclusion.

It appears to us that it is the duty of pharmacists to accept the responsibility placed upon them by this enactment and fulfill same in a professional spirit. The following sensible view of the situation is presented by George Victor Haering, of Chicago, in the *C. R. D. A. News* and republished in the *N. A. R. D. Journal*, of February 26, 1920:

"Inasmuch as the Government has recognized liquor as a medicine and a medicine only and left it to the discretion of physicians so to prescribe, and in its judgment realized that the registered pharmacist by virtue of his high standing as regards character, reliability and honesty was the one best qualified to dispense and handle same, I for one have taken out a license, realizing that many millions in this country believe sincerely in the medicinal virtues of liquor and I am not the judge, but merely the 'order taker' when filling aforesaid prescriptions written according to the precepts of the law.

"The confidence bestowed upon me by the Government in permitting me to dispense narcotics and liquors shall not be betrayed, as I fully realize the high honor thus bestowed upon me as a pharmacist as well as my duty as an American citizen."

G. M. B.

## THE FAULTS OF MEDICAL EDUCATION.

In this number of the JOURNAL we republish the paper of Hobart Amory Hare, M.D., on the "Teaching of Therapeutics," published in the *Journal of the American Medical Association*.

Our purpose in republishing this article is twofold. First, it is a frank statement by an eminent authority of a great fault in the current medical education. The neglect of the medical schools to impart to their students a sufficient medical education that will enable them to intelligently practice their important profession is a serious indictment of the educational methods employed in colleges of medicine.

Many pharmacists no doubt could relate instances of the lack of knowledge of materia medica and practical therapeutics exhibited by physicians, and by their experiences attest the truthfulness of the criticism of Prof. Hare that many of the young physicians entering medical practice have no clear understanding of posology and the true significance of a *dose*. The examples he gives in this article of the lack of acquaintance with official titles are duplicated in a great many of the prescriptions presented for compounding.

It is unfortunate that this arraignment of the lack of knowledge on the part of many physicians, and the faulty methods of teaching in vogue in medical schools is true.

The need for a more thorough and a more practical method of training the medical student to prescribe, and the plan suggested for correcting this defect, should receive the merited consideration, and likewise the necessity for having instruction imparted by those who have gained the knowledge they wish to impart through actual practice.

Our second purpose in republishing this paper is its applicability likewise as a lesson to pharmaceutical educators. To a more or less degree the same faults in the method of imparting knowledge by teachers utterly lacking in experience is, likewise, evidenced in many of the schools of pharmacy. Post-graduate courses in medicine or in pharmacy should be based on a *comprehensive knowledge* and prior education in the fundamental branches of these practices and reserved for specialists who will not only apply the knowledge acquired in post-graduate work, but extend the existing knowledge in these fields through their further practice and research therein.

It is not our purpose to cast any reflection upon our friends of

the medical profession. We are of the opinion that pharmacy has too many glass houses to safely engage in "stone-throwing," and the insufficiency of our pharmaceutical education is a topic that it is proposed to editorially discuss in an early issue. G. M. B.

#### FURTHER MODIFICATIONS OF THE REGULATIONS FOR PROHIBITION ENFORCEMENT.

In our editorial comments we have taken exception to the requirement of the regulation No. 60 that bay rum, hair tonics and other toilet preparations must be denatured by the addition of tartar emetic. Throughout the trades affected by this early promulgation of the Federal Prohibition Commissioner, there has been a very pronounced opposition to this ruling. The Department has now modified this in a mimeographed regulation known as Prohibition Mimeograph No. 38, which sets forth four additional optional modifying agents that may be used in place of tartar emetic. These are quinine sulphate 2 grains to the fluid ounce, cinchonidine sulphate 2 grains to the fluid ounce, salicylic acid 5 grains to the fluid ounce and resorcin, 5 grains to the fluid ounce.

It is not improbable that further consideration will justify the Department in admitting as modifying agents the use of some other denaturing agents than those now specified.

This Bureau has likewise issued as Prohibition Mimeograph No. 40, a regulation regarding the reports of liquor sold by druggists on physicians' prescriptions. This reads as follows:

"A report on Form 1418 has been prepared to be rendered by druggists and pharmacists each month, showing the number of prescriptions filled and the quantity of liquor sold on physicians' prescriptions.

"Form 1418 must be made in triplicate each month by the holder of each permit to dispense intoxicating liquor for medicinal purposes on physicians' prescriptions written on Form 1403, or on emergency prescriptions as authorized by law.

"Two copies of the report on Form 1418 must be sent by the druggist holding permit, to the Federal Prohibition Director of the State on or before the fifth day of month succeeding the month for which the report is rendered; one copy will be retained by the druggist rendering the report.

"Liquors used in compounding medicines should not be reported on Form 1418, as this form is intended to be a report solely of liquors

sold as such on prescriptions of physicians holding permits to prescribe liquor; medicinal preparations fit for beverage purposes should, however, be included in the report on Form 1418.

"The report of druggists on Form 1418 should not include sales of liquor to other druggists or to physicians or hospitals, except on authorized prescriptions, nor sales of liquor for industrial or scientific purposes; it should include only such liquors as are dispensed and sold on authorized prescriptions of practicing physicians to parties for medicinal use.

"One copy of the druggists' monthly report on Form 1418 will be retained by the Federal Prohibition Director, and one copy will be forwarded to the Federal Prohibition Commissioner at Washington, D. C., together with Form 1419.

"The Federal Prohibition Director will report each month on Form 1419, entering thereon the names and addresses of each druggist or pharmacist holding permit to dispense liquor on physicians' prescriptions. Upon receipt of Forms 1418 from druggists, the Director will enter on Form 1419 opposite the name of the druggist the number of prescriptions filled during the month, and the quantity of each kind of liquor sold.

"Report on Form 1419 should be rendered promptly each month, not later than the tenth day following the month for which it is rendered, notwithstanding the Director may not have received Forms 1418 from all druggists holding permits to dispense liquor on physicians' prescriptions. The name of each druggist holding such permit must be listed on Form 1419.

"When the quantity of liquor sold and the number of prescriptions filled cannot be entered on Form 1419 by reason of the failure of druggists to file Form 1418, the Director will not later than the last day of the month render a supplemental report on Form 1419 of all returns on Form 1418 received by him from druggists after his regular report for the month on Form 1419 has been rendered. The supplemental report on Form 1419 must contain a list of all druggists listed on the regular report and from whom no return on Form 1418 had been received when the regular report on Form 1419 was made by the Director. When a druggist has failed to file his return at the end of the month, action should be taken looking to the revocation of his permit, unless a good and sufficient reason shall be shown for the delinquency in filing his return.

"When a return on Form 1418 is not filed with the Director on or

before the tenth of the month by any druggist holding permit, the Director will call upon such druggist to render his return on Form 1418 at once.

"Report on Form 1418 by druggists will not be required for any month prior to March, 1920. Reports for March and for each month thereafter will be required to be rendered by each person holding permit to dispense liquor on physicians' prescriptions. If such permit is issued to any person during any month, a report must be rendered by the permittee for the remainder of the month after receiving his permit, and for each month thereafter during the life of the permit.

"When the Prohibition Director for the State is not yet appointed or whose office is not yet established, the Collector or Collectors of Internal Revenue in such State will be required to receive Forms 1418 from druggists and list the same on Form 1419.

"Before supplying druggists with blank copies of Form 1418, following the word "at" and under the words "To Federal Prohibition Director," the Director will write or stamp the name of the city and state where his own office is located, in order that druggists may be advised as to where the report is to be sent.

"Directors will note on the back of Forms 1418 the date when received from druggists. This notation may be made with a rubber stamp, care being taken to indicate clearly the date when received in the Director's office."

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## OBLIGATIONS AND METHODS OF RESEARCH.<sup>1</sup>

BY HENRY LEFFMANN, A.M., M.D.,

LECTURER ON RESEARCH, PHILADELPHIA COLLEGE OF PHARMACY.

The primary object of science is the determination of truth. It is not essential to this object that the truth shall have an obvious value to mankind. The study of the properties of magic squares is, from the purely philosophic point of view, as commendable as the study of the cause and cure of cancer. It is, however, the dominant feature of present science to make it "practical," that is, yielding data that can be turned to account either in increase of wealth or

<sup>1</sup> Abstract of an address delivered by invitation at a meeting of the Faculty of the Philadelphia College of Pharmacy, November 24, 1919.



increase of comfort and enjoyment. A strong contrast is to be noted between the relations of the ancient and modern scientists to their respective communities. In ancient times the scientist stood apart from the practical life, disdaining, as a rule, the investigation of agricultural and industrial problems. Socrates rebuked one of his disciples for suggesting that the study of astronomy might have practical value in navigation or otherwise. It is pursued, he said, as an ennobling influence. To-day, the cause of science is urged upon the public almost wholly on the basis that material benefits will result from it. The student who enters upon a course of study in any science, does so almost always with a practical application in view, and this is especially true of the students at professional schools. Hence, in the great mass of cases, we pass over the loftier aims of science, "pure science," as it is called, and take up the practical side, technically known as "applied science."

There is, however, one sentimental phase that must not be forgotten, namely, that there rests upon every scientific worker the duty of contributing something to the stock of knowledge. The vast mass of information now available is almost wholly the free contribution of previous workers, and every one who practices a profession that applies such information, or who pursues the study of science for itself alone, should bear in mind the previous workers who have handed the torch to him, and should feel the obligation to pass it on still brighter to those who come after him.

It is given, it is true, to but few mortals in any age, to be possessed of that special ability which we call genius. It is a term difficult to define. Perhaps the only definition available is the merely epigrammatic one that "genius is the infinite capacity for taking trouble." It is a great mistake, however, to assume that research can be conducted only by a favored few. Epoch-making discoveries constitute but a small part of the development of science, the greater part of its literature is minor detail, the value of which is cumulative. It is, therefore, within the power of all to add something to the store. Let me indicate some of the lines along which this may be done.

Every investigation should be preceded by a search in the literature. It will often appear that the line intended to be followed will be found to have been already surveyed if not actually opened. At every turn in science, we are apt to be impressed by the truth of Sydney Smith's remark about "those confounded ancients who anticipated everybody." I recall that some years ago I thought I

had devised a new method of obtaining photographs, the use of a gelatin film containing mercurous iodide. I deemed it best, however, to make some search in the matter and soon found the process had been published eleven years before I was born. It is still more disappointing to find out that some ancient Greek anticipated one in some discovery.

Yet an important observation must be made here, namely, that while the literature of science contains a very large mass of information, it must not be accepted without question. Experience shows that even the most capable of investigators may be seriously misled. This is due to several causes. Preconceived notions often blind ablest men to the real facts of the case. The mind too often perceives what it wants to perceive. Even in the material environment of the analytic laboratory, feeling and prejudice are not wholly lacking. A more frequent cause of error is, however, the imperfections of methods of research, and the lack of thoroughness of information. Much as one may be astonished in examining the literature of a given subject, at the anticipations in results, one is often equally astonished at how much is taken for granted, and how such assumptions form the basis of further investigations. A striking instance of this occurred in the experience of my co-worker, Dr. William Beam, and myself. We had devised a process of analysis which depended on the use of a strong sodium hydroxide in glycerol, with operation at a moderately high temperature. It was vital to the practical value of the process that no decided action should take place between the alkali and the solvent, especially that no substances of low volatility should be formed. Now Watt's Dictionary, a well-known and carefully compiled work, stated definitely that when glycerol is heated with strong alkali, salts of some of the lower fatty acids are formed. If this was true, the process was worthless. Careful experiment showed that it was not true. A good quality of glycerol heated well above the boiling point of water with strong sodium hydroxide solution gave no appreciable traces of any of these acids. The explanation of the error is probably that the original investigator used, unknowingly, an impure glycerol. The observation dated from an early period when the methods of preparing and purifying glycerol were but imperfectly known. Probably the application of the substance to the manufacture of high explosives, in which an exceptionally pure article is needed, led mainly to the improvement in the quality of the commercial

article. Another example of the liability of initial investigators to error is the fact that one of the first tests given for detection of benzene is due to a then unsuspected impurity—thiophene—in the commercial forms of benzene. When this impurity was detected, it was found that benzene freed from it does not give the reaction. Revision of earlier work is a promising field of minor research.

Any research of moment involves the preparation of a bibliography, the list of authorities consulted. Much reform is needed along this line and I hope those of you who are present will be crusaders in this cause. I am referring to the frequent imperfect and erroneous references that one often meets. The most serious omission is the year of publication. This is often the most important item in the matter, yet many authors neglect it. The volume number, if the journal has one—the edition-date in the case of a book—must not be omitted. Volume numbers should never be given in Roman characters. These are, indeed, not troublesome in the smaller amounts, but are exasperating above a score or so. The system has nothing to recommend it. British writers are very fond of it, but the leading British journal for abstracts in chemistry—*The Journal of the Chemical Society*—has long since discarded the practice and gives volume number in the common numerals called usually Arabic, but believed by many to be of Hindu origin. It is gratifying to note that some scientific journals have discarded altogether volume numbering, using merely the calendar year. This is a move in the right direction. In preparing a bibliography large or small, each reference should be verified if possible, if not, a statement that it is based on a secondary source should be noted. The several items of each reference should follow in a uniform order, that is, the year should not come first in one item and the volume first in another item. Uniformity in this respect gives neatness to the page and convenience to the user.

The English-speaking research worker in any important science should be reasonably familiar with French and German. I know, of course, that at present there is a feeling of dislike for anything that comes from the second source, but in this matter we must be guided by self-interest and not by feeling. The ancients knew the value of obtaining information from any source, and in the Latin proverb, "*Fas est, et ab hostis doceri*," "It is allowable to learn from the enemy," they expressed the view. Plutarch wrote an essay of the same tenor. Great Britain and France have set us examples in this

respect. Though they have both suffered much more severely than we have from the German methods of warfare, they have both decided to increase rather than diminish their studies of the literature of their late enemy.

Speaking as I am on this occasion to those engaged in active teaching work, I feel that research in methods of teaching deserves special notice, especially as it is often overlooked. There is, in fact, at the present time, a tendency to minimize the lecture as a method of instruction, and to lay stress almost wholly on the laboratory and the practical side. I believe this to be an error. There is no attribute of humanity higher than intelligent speech, and there is no method better adapted to secure and maintain for a reasonable time the attention of a group of students than a well delivered lecture. I have long felt that our preparatory institutions, particularly those engaged in the training of teachers should devote much more time than is now devoted to instruction in lecturing. This cannot be obtained by the practice of reciting prose or poetry from some standard collection but must consist in exercises in speaking without notes, or at least with only outline notes, upon some topic for which the speaker has made special preparation. A crowd, whether of hoodlums or post graduates, has always something of the nature of a collection of wild animals into which the speaker enters. His safety lies largely upon keeping his eyes upon them. In lecturing, clear utterance, careful selection of phrases, simple language, are important. It is impossible to avoid technical terms in scientific teaching but in many cases ordinary words will serve. Illustrations of points by experiment are necessary but may be easily overdone. As far as the physical sciences are concerned, the laboratory hours afford the student much opportunity to perform illustrative experiments, so that the lecturer can give more time to explanation and direct statement. The modern extensive use of the lantern has one serious drawback—it keeps the room dark, thus taking away the supervision of the teacher and also interfering with note-taking.

These are some suggestions offered as a brief summary of the aid that can be rendered to the advancement of knowledge by those who have taken up its study and practice. The opportunities are immense. They are by no means limited to the abstruse and elaborate investigations that are now so regularly contributed by leading scientists. The nature of the atom and of force, the existence and properties of the ether, the exact determination of atomic weights,

these are problems that require extensive equipment, long training and special aptitude, but they constitute only a small portion of the field which is everywhere ripe to the harvest, and in which the humbler gleaner, with ruder tools can labor with benefit to science, both in its abstract and applied phases.

It is, as I said in the beginning, the duty of all to help in collection of data, either by adding new facts or correcting old statements or even classifying known data, and rendering them more easily understood or more accessible. Research should be undertaken intelligently, that is, with some clear object in view. It is true that some few important discoveries have been made by what seems to be accident, but it will be found that in most cases the discoverer was engaged in real and commendable investigation, and was not merely working at random.

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## NOTES ON SOY BEAN UREASE.

BY ARTHUR W. DOX, PH.D.,

IOWA STATE COLLEGE, AMES, IOWA.

An enzyme capable of decomposing urea into ammonium carbonate was discovered in soy beans by Takeuchi<sup>1</sup> in 1909. Four years later Marshall<sup>2</sup> worked out a quantitative method for the determination of urea in urine by means of soy bean extracts. The method consists essentially in titrating the ammonia formed by the action of the soy bean extract upon the urea solution, using methyl orange as an indicator. Under the conditions described, the reaction was quantitative in three hours. A slight error, amounting to 0.8 per cent., due to carbon dioxide, was considered negligible in clinical work. In a second paper, Marshall<sup>3</sup> adapts the method to the determination of urea in blood, collecting the ammonia by aeration. Later, he<sup>4</sup> studied the activity of soy bean extracts, as affected by dilution, acids, alkalies and ethyl alcohol.

The properties of soy bean urease have been studied extensively

<sup>1</sup> *Jour. Coll. Agr. Tokyo.*, 1: 1, 1909.

<sup>2</sup> *Jour. Biol. Chem.*, 14: 283-90, 1913.

<sup>3</sup> *Ibid.*, 15: 487-94, 1913.

<sup>4</sup> *Ibid.*, 17: 351-61, 1914.

by Van Slyke and Cullen.<sup>5</sup> They found the optimum temperature to be about 55° C. Thirty minutes' heating with water at 60° was without effect, 30 minutes at 70° destroyed about one-fourth of the activity, and at 80° there was complete inactivation. Hydrolysis of urea by urease is not reversible.

It is not the purpose of this paper to review all of the literature. Commercial preparations of purified urease are now on the market and are being used extensively in urine analysis. In general it appears that urease is most abundant in seeds of high protein content, particularly in the Papilionaceae. Its absence, however, has been reported in beans, peas, cowpea, velvet bean and sweet pea.

Incidental to a study of various seeds to discover a possible correlation between enzyme activity and germinating power, the writer had occasion to compare the urease content of a number of soy beans of different varieties and germinating power. The only published work along this line appears to be that of Annett,<sup>6</sup> who examined six varieties of soy beans which he describes as yellow, cinnamon, chocolate, spotted, black and Rymbsa Ktang. His method consisted in treating 10 g. of powdered seed with 100 Cc. distilled water in the presence of toluene for one hour at room temperature. Two Cc. of the extract were added to 50 Cc. of a 1 per cent. urea solution, the mixture kept at room temperature (about 27° C.), and 5 Cc. aliquots titrated at half-hour intervals, using methyl orange as an indicator. The six varieties showed striking uniformity.

In the present work, 5 Gms. of each sample of soy beans were ground in a mortar and worked through a 40-mesh sieve. One-tenth of a gram of the powder was placed in a small Erlenmeyer flask, 15 Cc. distilled water at 40° added, then 10 Cc. of a 1 per cent. urea solution, after which the flask was stoppered and placed in a constant temperature bath at 40°. For purposes of comparison it was decided to allow the reaction to proceed for a period of time sufficient for the hydrolysis of about one-half of the urea. From the following table it will be seen that this point is reached in about 30 minutes. At intervals of ten minutes, one of a series of flasks containing the above mixture was removed from the bath and titrated with decinormal hydrochloric acid, using methyl orange as an indicator. A uniform blank of 0.6 Cc. was deducted in each case.

<sup>5</sup> *Jour. Biol. Chem.*, 19: 141-80, 1914.

<sup>6</sup> *Biochem. Jour.*, 8: 449-52, 1914.

TABLE I.

Seed No. 162,806. 0.1 Gm. powdered seed, 15 Cc. H<sub>2</sub>O, 10 Cc. 1 per cent. urea solution, temperature 40°.

Time in minutes.	Cc. N/10 HCl.	Time in minutes.	Cc. N/10 HCl.
5	3.6	70	26.3
10	6.7	80	28.5
20	10.9	90	30.2
30	14.8	100	31.6
40	18.2	110	32.7
50	21.3	120	33.2
60	24.2	130	33.2

The theory for 10 Cc. of 1 per cent. urea is 33.3 Cc. The reaction was therefore quantitative in two hours under the conditions of the experiment.

It remained to be determined whether the method of preparation of the sample by grinding and sieving was sufficiently uniform for comparative tests. Each of the preparations used in the following experiment was ground separately.

TABLE II.

0.1 Gm. powdered seed, 15 Cc. H<sub>2</sub>O, 10 Cc. 1 per cent. urea solution, temperature 40°, time 30 minutes.

Seed No.	Cc. N/10 HCl.	Seed No.	Cc. N/10 HCl.
162804	15.9	163115	11.4
162804	15.6	163115	11.1
162804	15.9	163115	11.3
162806	14.4	163115	11.3
162806	14.5		
162806	14.4		
162806	14.8		

It is evident from the above that the method of preparation used is applicable for purposes of comparison, the greatest variation observed being 0.4 Cc. for different preparations of the same sample.

As might be expected, the velocity of the reaction increases with rise in temperature, as shown in the following experiment.

TABLE III.

Seed No. 162,902. 0.1 Gm. powder, 15 Cc. H<sub>2</sub>O, 1 Cc. 1 per cent. urea, time, 30 minutes.

Temperature.	Cc. N/10 HCl.	Temperature.	Cc. N/10 HCl.
20	5.2	50	20.8
30	8.5	60	25.0
40	14.9		

The greatest activity is at a temperature above 50° and probably below 60°. Van Slyke gives 55° as the optimum.

In comparing the activity of the different seed samples, 0.1 Gm. of the powdered sample was used in each case, 15 Cc. water and 10 Cc. of a 1 per cent. urea solution. After 30 minutes in a bath at 40°, the mixture was titrated and a blank of 0.6 Cc. deducted. In addition to germination tests, nitrogen and moisture were determined in the samples. Results are given in the following table. The samples were all of the 1918 crop, with the exception of *a* and *b*, which were grown in 1914.

TABLE IV.

Seed No.	Variety.	Cc. N/10 HCl.	Germin- ation %.	Nitrogen %.	Moisture %.
151415	Black Eyebrow	20.2	87	....	....
151413	Black Eyebrow	19.7	73	6.35	6.24
151421	Black Eyebrow	19.1	80	7.12	6.01
151416	Black Eyebrow	19.1	41	6.44	6.18
151417	Black Eyebrow	18.6	70	7.16	6.36
151412	Black Eyebrow	18.5	75	7.49	6.36
163336	Black Eyebrow	17.1	61	7.66	6.39
163371	Black Eyebrow	17.0	52	7.67	6.15
163102	Manchu	17.0	92	6.77	5.99
163342	Black Eyebrow	16.9	31	7.47	6.31
<i>a</i>	Mammoth Yellow	15.6	2	7.11	5.97
162806	Minn. 109	15.2	95	7.41	5.51
162801	Minn. 109	15.2	91	7.30	6.15
162804	Minn. 109	15.1	89	7.48	5.60
162905	Minn. 110	15.0	75	7.28	5.96
162902	Minn. 110	14.9	51	7.02	6.08
151418	Black Eyebrow	14.8	82	6.49	6.04
161201	Ohio 7403	14.2	93	7.50	6.03
161119	Ohio 9100	14.1	95	7.91	6.24
161101	Ohio 9100	13.4	92	7.37	6.05
163115	Manchu	11.3	87	7.05	5.93
<i>b</i>	Wilson	11.1	23	6.68	6.23

From the above, it is evident that in the intact seed the urease is very stable, and as far as these observations go, its activity bears no relation to the germinating power of the seed, nor to the nitrogen or moisture content of the latter.

Fifteen varieties of soy beans, all of the 1919 crop, were then tested in the same way.



TABLE V.

Variety.	Cc. N/10 HCl.	Germination %.	Nitrogen %.	Moisture %.
Columbia.....	18.9	71	7.05	5.98
Black Eyebrow.....	18.9	73	7.75	5.54
Chestnut.....	17.4	82	6.30	6.15
Mandarin.....	17.4	51	7.92	6.26
Wilson.....	17.3	81	7.92	6.05
Morse.....	17.0	82	7.58	5.50
Jet.....	17.0	84	9.26	6.80
Black Sooty.....	16.8	80	7.42	6.30
Ito San.....	16.7	87	7.98	5.69
Elton.....	15.9	73	7.84	6.35
Wisconsin Black.....	15.7	57	8.26	6.16
Ebony.....	14.6	67	8.31	6.41
Ia. 150110.....	14.1	80	7.89	6.11
Minn. 166.....	14.1	51	7.61	6.12
Manchu.....	13.6	98	8.09	5.36

It will be seen that some difference exists in the urease activity of different varieties of soy beans, but this difference appears to bear no relation to the germinating power of the seed or to the protein content of the latter. In fact urease may be demonstrated in seeds that are practically dead, as in the case of sample "a," Table IV.

The writer is indebted to Mr. J. H. Christ, of the Farm Crops Dept. of Iowa State College, for making the germination tests.

## CANTHARIDES ASSAY.

By LOUIS DU BOIS,

NEW BRUNSWICK, N. J.

The U. S. P. prior to the present IX edition, contained no standard for cantharides and no method for assay.

For years we have been using in this laboratory a method for the determination of the free cantharidin content of cantharides, which had been evolved from sources mentioned elsewhere in this article. This method has appeared to give satisfactory results both in the concordance of the results and in the apparent purity of the resulting crystals.

The report of work along this line, as given herein, is by no means final, but it has been considered advisable to publish it for the obvious reason that the U. S. P. method now official and the results from its use seem to be so unsatisfactory in our hands that we believe the matter has not been given the attention it deserves.

U. S. P. Method.

15 grams.

150 Mils. of a mixture of 2 parts of benzene and 1 part purified petroleum benzin.

2 Mils. HCl.

Let stand over night. Gradually warm to 40° C. and keep there 3 hours, with frequent shaking. Cool and decant off 100 Mils.

Evaporate to about 5 Mils.

Add 5 Mils. CHCl<sub>3</sub> and let evaporate in warm place.

Add 10 Mils. of a mixture of equal parts of dehydrated alcohol and purified petroleum benzin saturated with pure cantharidin, let stand 15 minutes. Decant liquid through a pellet of purified cotton and reject filtrate.

Wash crystals with successive portions of saturated cantharidin solution, prepared as directed above, until free of coloring matter, and pour through the same pellet of cotton.

Wash cotton with small amount hot CHCl<sub>3</sub> and add washings to tarred beaker.

Evaporate solvent.

Dry 1/2 hour at 60° C.

Weigh.

Resulting weight equals cantharidin in 10 grams of cantharidin.

This should give both free and combined cantharidin.

METHODS USED.

Author's Method.

10 grams.

30 Mils. CHCl<sub>3</sub>.

Let stand over night.

Shake during several hours.

Filter and wash with 70 Mils. CHCl<sub>3</sub>.

Evaporate on water bath.

Treat residue with 5 Mils. CS<sub>2</sub>.

Transfer to small tarred filter paper, 4 cm. diameter.

Wash with 10 Mils. CS<sub>2</sub> in small portions.

Dry filter at 60° C.

Weigh.

Add 0.010 grams for solvent action of CS<sub>2</sub>.

This should give free cantharidin.

To obtain combined as well, add 2 Mils. HCl to the original chloroform.

Bandin's Method.

25 grams.

100 Mils. CHCl<sub>3</sub>.

Let stand over night.

Shake 2 to 3 hours.

Filter on covered filter. Collect 60 Mils. of the filtrate representing 15 grams.

Evaporate on water bath, and proceed just the same as the Author's Method.

This should give free cantharidin. To obtain combined as well, add 2 Mils. HCl to the original chloroform.

The assays were run on two different lots of cantharides used in our manufacturing department.

*First Lot:*

U. S. P. Method.....	0.71% free and combined cantharidin
Author's Method.....	1.17% free cantharidin

*Second Lot:*

U. S. P. Method.....	(a) 0.569% free and combined cantharidin
	(b) 0.570% free and combined cantharidin
Author's Method.....	(a) 0.795% free cantharidin
	(b) 0.810% free cantharidin
Baudin's Method.....	(a) 0.789% free cantharidin
	(b) 0.753% free cantharidin
Author's Method Modified....	(a) 1.73% free and combined cantharidin
	(b) 1.77% free and combined cantharidin

The method pursued in this laboratory is the one given here under the heading "Author's Method." It is the assay method of Baudin as given in Hager's "Handbuch der Pharmaceutischen Praxis," Vol. I, page 595, and in Sadtler and Coblenz's "Pharmaceutical and Medical Chemistry," Vol. 2, page 226, modified only so as to make it a complete extraction method, instead of an aliquot portion method. We have nothing now to suggest as to the relative value of these two well-known chemical procedures except to express a preference for total extraction methods. This does not seem to agree with the trend of development of the U. S. P. text.

A glance at the U. S. P. will leave no doubt that the cantharides assay is a very troublesome and difficult procedure. Note the digestion, maintained at 40° C. for three hours with frequent shaking. Note the evaporation to about 5 Mils. and the addition of chloroform to promote crystallization. Note the curious mixtures of solvents used—benzene and benzin, dehydrated alcohol and benzin.

However, the chief objection that we have found with the U. S. P. assay method is not the number of manipulations and varieties of solvents involved, but that we have been obtaining lower results for both "combined and free" cantharidin, by this method than we obtain for "free" cantharidin alone by either the Author's or the original Baudin Method; and that the resulting crystals are not as satisfactory as those obtained by the latter two methods. The crystals obtained by both the Author's Method and Baudin's Method for free cantharidin are clean, white and well formed. Those we have obtained with the U. S. P. assay method have been dark and resinous.

We have also run assays for total cantharidin (both free and combined) by modifying both the Author's Method and the method of Baudin, by the addition of 2 per cent. of hydrochloric acid to the first solvent. The results by these methods are still higher, but the crystals obtained are not as satisfactory as those by the methods for free cantharidin alone—the resulting crystals not being as pure and free from resinous matter.

The U. S. P. makes no reference to the presence of both free and combined cantharidin in cantharides; but the assay given is for both the free and combined, hydrochloric acid being added to liberate the alkali-combined cantharidin.

We have never seen any published statement as to whether the combined cantharidin has any blistering effect when applied to the skin, but have assumed heretofore that the blistering effect is due to free cantharidin alone, when the powdered cantharides is used as an ingredient of a blistering plaster. It would seem that this also is believed to be true in the case of the official tincture where no attempt is made to liberate the combined cantharidin before making the alcoholic extraction. On the other hand, acetic acid has been incorporated in the formulas of the other two official cantharides preparations, *Ceratum Cantharidis* and *Collodium Cantharidatum*.

RESEARCH LABORATORY,  
JOHNSON & JOHNSON,  
NEW BRUNSWICK, NEW JERSEY.

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## PEPSIN ADSORPTION BY CHARCOAL.

BY NORMAN D. KEEFER, P.D.,

PHARMACIST, PENNSYLVANIA STATE SANATORIUM FOR TUBERCULOSIS,  
MONT ALTO, PA.

Adsorption, as a phenomenon, has been practiced for centuries, but it has only been for the last quarter century that it has been understood. Adsorption is a condition of distribution, wherein the surface rather than the dispersed phase plays the important rôle. We know that bone black is used to bleach dark sugar juices, extract fusel oil from alcohol, and decolorize dark solutions of the organic chemist. And now we are to learn that any substance which causes a marked diminution of surface tension of water, such as fats, soaps, albumin, etc., are very readily absorbed.

Since powdered charcoal is a very good adsorbent, we will start our attack upon it and its common accomplice, in the medical profession. Charcoal and pepsin is a very frequent combination dispensed by prescriptionists, as well as put up in tablet and capsule form by wholesalers. While it is advised therapeutically that pepsin be given alone and not in combinations for fear of its chemical incompatibility; in this instance no chemical reaction occurs, but an adsorption of pepsin by the charcoal as soon as the two substances are moistened.

To prove this adsorption, two samples of pepsin, a powdered and a granular grade, were first tested by the U. S. P. method of assay and found to be of 1 : 3000 strength or U. S. P. As our present day pepsin is an enzyme in combination with albumin (mostly albumin) it will readily give an albumin test, when the top layer of an acid solution is heated in a test tube over a flame. (Same as heat test for albumin in urine.) By filtering this acid solution, which is of pepsin and acid strength according to U. S. P. assay, through charcoal, the filtrate will be free from albumin. This charcoal-filtered solution was tested on freshly-coagulated albumin according to U. S. P. assay and found to assay 1 : 300. This value, I believe, could be lowered considerably, by better filtration as only ordinary filter paper was used.

Next a group of tests were made with 0.5 Gm. of charcoal in 100 Mils. of the U. S. P. test solution. This charcoal-containing solution assayed to about 1 : 500 as near as could be estimated; the charcoal making the end reaction indistinct. This group of tests was made to ascertain what action might be expected to occur in the stomach, when about the same proportions of each drug are dispensed in tablet form.

Since this adsorption by charcoal is a very rapid process, it can be readily seen that pepsin-charcoal combinations, in tablet or capsule form, will as soon as moistened (in the process of dissolving) begin the adsorption reaction. An easy example of this can be shown by dissolving a few charcoal and pepsin tablets in 0.2 per cent. hydrochloric acid, filtering the solution, and testing filtrate for albumin; this will prove the albuminous enzyme is absent.

From these experiments and deductions it can be readily seen that all our former therapeutics concerning these two drugs, when used together, has been at fault.

While on this subject of adsorption, it might be well to state some

of the more recent uses of charcoal as an adsorbent. Charcoal was used very extensively in the war as an adsorbent in the gas-mask. It was also used in the treatment of severe enteric infections such as cholera, dysentery, and typhoid. The results were very gratifying, for it not only acts as an adsorbent of toxins produced by the infectious agent, but by adsorbing the bacteria themselves. Charcoal in large doses has yielded good results in hyperchlorhydria and fermentation. Lichtwitz overcomes obesity by administering charcoal in such amounts to satisfy the pangs of hunger, and at the same time it removes the acids and enzymes from the system, and diets the patient. Sterile charcoal has been used in purulent and dissection wounds as well as in exuberant carcinomata.

A good effect was obtained by administering charcoal impregnated with iodine and thymol in the treatment of typhoid. A preparation of charcoal impregnated with sulphur is used as a mild laxative, which at the same time relieves flatulence by adsorption of putrefactive material and bacteria.

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## A MODIFIED FORMULA FOR MAGMA MAGNESIA.

BY BERTHA MUELLER,

ASSISTANT PHARMACIST AT THE LANKENAU HOSPITAL, PHILADELPHIA, PA.

At the present time, pharmacists are being invited to give helpful suggestions for the coming pharmacopoeia, in order to make the book even more successful than its predecessors have been. It might be pertinent, therefore, to point out that one of the greatest factors contributing toward such success must perforce be simplicity in technic of working-formulas.

The manufacture of pharmaceutical preparations constitutes a most interesting piece of work, and it cannot be reiterated too often that pharmacists ought to do as much of their own manufacturing as possible, if for no other reason than that of pleasant diversion from dull routine. And pharmacists, no doubt, would do more of their own manufacturing if it did not in many instances involve an undue amount of time and labor to make a comparatively simple preparation. Hence, it has ever been the ambition of the writer to try to simplify the technic in complicated working-formulas wherever it

seemed possible to do so without harmful effect on the finished product.

This has again led to some work on Magma Magnesia. This preparation promises to become ever more popular as time goes on, and it must be conceded that neither of the two formulas that have been made official are entirely satisfactory because they involve too great an expenditure of time, money, and labor. It is not the writer's object to go further into detail on this point than to draw attention to the fact that the one great drawback in these formulas is the washing process. It is costly and time-consuming.

A pharmacist must either prepare the water for washing the magma or he must use distilled water. The former involves time and labor; the latter expense. Since pharmacists usually buy their distilled water, they would hardly feel that it pays them to use it in such immense quantities as are required for the washing of this preparation. A formula, therefore, that does away with this washing process should prove of considerable value. Such a formula was advanced some years ago by F. C. Weber, who, according to the *Proc. of the P. P. A.*, for 1915, mentions Calcined Magnesia as yielding a satisfactory magma, and gives formula and directions for preparing the same.

Light Magnesium Oxide U. S. P. is without doubt a most satisfactory chemical for this purpose. It yields a magma which stands up splendidly, does not cake on long standing, pours easily, is beautifully smooth and white and is free from disagreeable taste. It must be remembered, however, that in order to have good results the chemical must be of U. S. P. standard.

The simplified formula advanced was tried out by us at the time; but it was not wholly satisfactory because of the property possessed by light magnesium oxide to gelatinize when mixed with water *per se*. This is a disadvantage, as the solidified mass thus formed is not easily broken up into a smooth magma. In order to overcome this undesirable feature, experiments were carried on with water containing a small percentage of some chemical. Various chemicals were tried out in that way. Ultimately it was found that lime water U. S. P. was the best solution for the purpose, as it prevents gelatinization and in its stead brings about a gradual thickening of the mixture.

The following formula has been used by us for some time and has always given satisfactory results:

Light Magnesium Oxide, U. S. P.....	60.00
Lime Water, U. S. P. to make.....	1000.00

Gradually and with constant stirring add the light magnesium oxide to about 800 Mils. of lime water contained in a graduate or a graduated wide mouthed jar. Mix thoroughly and bring up to 1000 Mils. with lime water, then pour into a bottle of the capacity of about two liters. Stopper the bottle and shake vigorously, at frequent intervals, until the mixture has thickened properly.

It has been our experience that vigorous shaking at frequent intervals hastens thickening of the magma. This is especially true if a bottle is used that holds considerably more than the amount of magma to be manufactured. If these requirements are carried out a splendid magma can be prepared within three days' time. It does seem strange, but it is a fact that rubbing the magma up in a mortar does not hasten its thickening nor is the finished product in any way superior to the one prepared according to above directions.

Another thing that might prove of interest is the corking of magma magnesia. It is common knowledge that ordinary corks are quickly acted upon by the alkaline mixture, causing them to turn dark, with the result that the magma is stained dark where it comes in contact with the cork. This unsightly appearance in the neck of the bottle can be avoided if the cork is given a protective coating of paraffine previous to its use. A cork thus protected can be used for months without causing the slightest discoloration.

It may be stated that though this chemical is much more expensive than magnesium sulphate, the quantity required for one liter of the preparation does not cost more than the sum total of the chemicals that enter into the same amount of magma prepared according to either of the formulas that have been officially recognized. This striking fact was brought out by an estimate made according to a price list for February, 1920, issued by a large chemical manufacturing firm. According to this price list, the cost of the chemicals for one liter of magma magnesia, U. S. P. formula, amounts to from twelve and one-half to thirteen cents. The cost of the chemicals according to the N. F. formula amounts to about fifteen cents, and that of the formula given above to about twelve and one-half cents. From this it can readily be seen that the distilled water required for washing the magma comes very much higher than the chemicals do.



## SUGGESTIONS FOR THE REVISION OF THE NATIONAL FORMULARY, FOURTH EDITION.

BY GEORGE E. ÉWE,

PHILADELPHIA, PA.

We are approaching the regular period for a revision of the National Formulary, and therefore suggestions for revision are pertinent at this time.

The present edition has rendered almost perfectly satisfactory service as a standard for the quality of the materials used in the compounding of medicinal preparations, which enjoy common usage, and as a standard for the methods of compounding and standardizing these preparations. So satisfactory has been that service, that it is with hesitation that I take up the task of presenting a few criticisms of the present edition, and also some suggestions for improvements for consideration in connection with the coming revision.

Absolutely no important defect in the present edition has presented itself to the writer. The suggestions made in this paper relate chiefly to minor improvements which may be of assistance in permitting the next edition to render even more satisfactory service than the present one.

### ADMISSIONS.

Upon the matter of admissions, very much can be said. Suggestions from individuals for admission of specific preparations and substances, in the absence of a general concurrent opinion, necessarily carry but little weight. A broad scientific method of accurately ascertaining the need of admitting items is urgently required.

The following plan is herewith submitted with the belief that if put into operation more accurate information regarding appropriate admissions into the N. F. will be ascertained than is possible through suggestions by individuals or organizations of limited scope:

*In the Case of Chemicals: Data for basing decision for admission.*—Lists of *purchases* of chemicals by the large and more representative drug trade jobbers and pharmaceutical manufacturers should be obtained. The output of chemical manufacturers should not be included unless the manufacturer supplies only medicinal chemicals or unless the manufacturer presents a list showing only his output of medicinal chemicals.

The lists should include all N. F. and all important and widely demanded chemicals, and *must be kept strictly confidential by the Revision Committee*. Purchases by jobbers and pharmaceutical manufacturers are suggested because these records are readily available, whereas *output* could not be obtained because of the diversions of a lot of chemicals to innumerable uses. A period of not less than two years should be considered as a basis for collection of data, as this is required to obtain an average.

Basis of decision: The items on the individual lists should be placed in classes based upon their dosage. Where output or purchase of non-official chemicals is greater than the output of N. F. chemicals of the same general dosage, the non-official chemicals should be placed in a class to be considered for admission to the N. F. Then the results of classification of all of the individual lists should be harmonized and chemicals thus selected should be seriously considered for admission to the N. F.

*In the Case of Crude Drugs: Data for basing decision for admission.*—Lists of purchases of crude drugs by larger drug trade jobbers and pharmaceutical manufacturers should be obtained. The output of a collecting house should not be considered unless the output is solely for medicinal purposes or the list specifies only the part of the output which was diverted to medicinal purposes. The lists should include all N. F. and all important and widely demanded crude drugs and *must be considered strictly confidential by the Revision Committee*. Purchases by jobbers and pharmaceutical manufacturers are suggested for the same reasons as mentioned under "chemicals" above. A period of not less than two years should be considered as a basis for collection of data, in order to obtain an average, because some supplies of crude drugs are purchased quite infrequently.

Basis of decision: As mentioned above, under "chemicals."

*In the Case of Pharmaceutical Products: Data for basing decision for admission.*—Lists of purchases by jobbers and output of manufacturers. The lists should include all N. F. and all important and widely demanded products, and *must be considered strictly confidential by the Revision Committee*. Purchases by jobbers and output of manufacturers are suggested, because these records are readily available. A period of not less than two years is desired for the collection of data, because the number of lots of any one preparation made up during one year is too small for average purposes.

Basis of decision for admission: Same as above under "chemicals."

In choosing the manufacturers and jobbers for coöperation in this plan, efforts should be made to have all sections of the United States and its possessions represented.

This plan is dependent entirely upon the acquisition of the coöperation of drug manufacturers, collectors, and jobbers.

Coöperation may possibly be obtained from many manufacturers, collectors, and jobbers upon formal request. Information offered must necessarily be considered *strictly confidential* and public acknowledgment of the assistance rendered should be made by the *Revision Committee*.

#### DELETIONS.

A broad scientific plan of ascertaining the advisability of deleting items from the N. F. is also urgently needed. Such a plan would result from the adoption of the above-mentioned plan for ascertaining the need for admitting items, as those N. F. items enjoying only small output by manufacturers and small purchases by jobbers, in comparison with the items being heavily manufactured and purchased, would naturally become candidates for deletion.

#### METHOD OF KEEPING THE N. F. WITHIN EASILY HANDABLE SIZE.

The less potent, less important, and less commonly used substances could be continued in the following edition, merely by name and by referring to the previous edition for descriptions of the methods and tests. Any required additional tests, or modifications of previous tests could be included under the name in the following edition and any deletions of previous tests could also be recorded there.

#### CHEMICALS.

*Manganese Glycerophosphate Soluble.*—This product consists of a mixture of 70 parts of Manganese Glycerophosphate and 30 parts of citric acid. Manufacturers of Manganese Glycerophosphate object to mixing their product with citric acid, therefore this product is not generally available. A formula for its manufacture should be included in the N. F. and the present monograph for this product should be adapted to plain Manganese Glycerophosphate, which also should be admitted to the N. F.

*Quinine Formate.*—The use of this substance is rapidly increasing and standards should be established for purposes of uniformity.

The majority of quinine formate on the market contains water of crystallization equivalent to about 5 per cent. of its weight. The melting intervals vary greatly. The quinine content is perfectly satisfactory, as all samples assay 100 per cent. or slightly over, of anhydrous quinine formate when the salt is dried at 100° C. and assayed for quinine alkaloid.

The following results were obtained on 6 lots examined during the past two years:

Sample No.	Loss at 100° C.	Melting Interval.
1	.....	120-122° C. (Not dried)
2	.....	124-126° C. (Not dried)
3	.....	145-150° C. (Not dried)
4	5.32%	169-171° C. (Dried)
5	5.00%	155-156° C. (Dried)
6	4.20	153-154° C. (Dried)

CRUDE DRUGS FOR WHICH NO PRACTICAL CHEMICAL OR PHYSIOLOGIC  
METHODS OF STANDARDIZATION ARE AVAILABLE.

Standards based upon the amount of soluble matter, extracted by the menstrum used in preparing fluid extract or tincture from the drug, should be adopted in order to establish uniformity in the use of these naturally variable medicinal substances. Limits which will include all natural variations should be established and an average adopted upon which the proportionate use of the drug must be based. These standards constitute the familiar "extractive standards" and no difficulty should be experienced by the Revision Committee in obtaining satisfactory data for the establishment of these standards, from the scientific laboratories of pharmaceutical manufacturing companies, who exercise scientific control of manufacture and also from other scientific sources.

EXTRACTS.

*Extract Euonymus.*—Very little of this extract is used and deletion is suggested, or continuance in the next edition by name only with reference to the present edition.

*Extract Hematoxylon.*—The remarks under Extract Euonymus also apply to this Extract.

*Extract Jalap.*—An assay process and standard might be included in the next edition for this product, for the purpose of establishing uniformity in market supplies.

The following process based upon the U. S. P. assay process for Jalap has yielded excellent results:

Assay for total resins: Sample about 2.5 Gms., accurately weighed. Place the sample in an Erlenmeyer flask; add 75 Mils. of 95 per cent. alcohol and heat on steam bath for four hours, using a funnel in the neck of the flask as reflux condenser. Wash into a 100 mil. volumetric flask, cool, dilute to 100 Mils. with 95 per cent. alcohol, mix well, filter and place 20 Mils. of the filtrate (equivalent to  $\frac{1}{5}$  of the sample originally weighed out) into a separator and finish like Jalap U. S. P.

Standard: Years of experience has shown that 28 per cent. total resins is a perfectly satisfactory standard, is practically attainable, and the trade is familiar with the therapeutic strength of an extract containing this percentage of total resins.

*Extract Podophyllum.*—Standardization of this extract is to be desired in order to establish uniformity in market supplies.

The following method has yielded satisfactory results for purposes of standardization, but it does not yield total results as explained below:

Sample about 2 Gms., accurately weighed. Boil in 20 Mils. of alcohol until dissolved. Filter, if necessary. Evaporate the filtrate in a 200 Mils. beaker to the consistency of a thin syrup. Pour 10 Mils. of ice water, containing 0.1 Mil. of concentrated hydrochloric acid into the thin syrupy concentrate and stir until all the lumps of resin disintegrate. Immediately filter off the precipitated resin while still ice cold on a counterpoised filter using *suction*, and wash the beaker, resin and filter with not more than 25 Mils. of ice water. Dry the filter and resin on a watch glass at 100° C. to constant weight.

This assay process is exactly similar to the U. S. P. assay method for podophyllum, with the exception that it is arranged for analytical procedure instead of for manufacturing procedure, and the resin is finally dried at 100° C. instead of being allowed to dry spontaneously. The spontaneous drying of this resin is a tedious and needless process, since air-dried podophyllin contains only around 4 per cent. of moisture as a rule. I have ascertained this by determining the moisture in many commercial lots of U. S. P. resin podophyllin, and have also determined it by permitting resin podophyllin obtained upon assay of this extract to dry spontaneously and then running a moisture determination on it.

This resin precipitation method is not all that could be desired since it consists of the precipitation of a partially water-soluble resin by water, and therefore the results are low. A much more accurate and consistent method is the "shake out" method proposed for Fluid Extract Podophyllum by W. M. Jenkins in *The Journal of Industrial and Engineering Chemistry*, p. 671, 1914. This "shake out" method gives higher results than the precipitation method, because total results are obtained and the resultant resin answers all U. S. P. requirements for Resin Podophyllin.

A perfectly satisfactory standard is: 17 per cent. resin. This standard is based upon practical attainment, and the trade is familiar with an extract of this strength.

#### FLUID EXTRACTS.

FLUID EXTRACTS FOR WHICH NO PRACTICAL CHEMICAL OR PHYSIOLOGIC METHODS OF STANDARDIZATION ARE AVAILABLE.

Standards based upon the average amount of soluble matter extracted from the drug by the menstruum should be adopted in order to establish uniformity in market supplies. These standards constitute the familiar "extractive standards," and no difficulty should be experienced by the Revision Committee in obtaining satisfactory data for the establishment of these standards, from the laboratories of pharmaceutical manufacturing companies who practice scientific control of manufacture and also from other scientific sources.

*Extract Chirata.*—There is practically no demand for this product and deletion is suggested or continuance in the next edition by name only and reference to the present edition.

*Fluid Extract Conium.*—The substitution of sulphuric acid for the acetic acid of the present formula and direct percolation to yield, is to be recommended.

The use of  $2\frac{3}{4}$  per cent. of a 10 per cent. solution of sulphuric acid has been found superior, in practice, to the acetic acid now prescribed, as the sulphuric acid is not volatile and holds the alkaloid in solution more efficiently. Slow, careful, direct percolation to yield gives practical exhaustion when acetic acid is used, as any alkaloid extracted by extra percolation will be largely lost when the extra percolate is concentrated in preparation for its addition to the bulk of the percolate.

When sulphuric acid is employed, extra percolation may be

productive of benefit, but even then it is usually more practical to merely obtain the yield of fluid extract by slow, careful, direct percolation to yield.

*Fluid Extract Cubeb.*—An assay based on the U. S. P. process for the determination of "volatile extractive, soluble in ether," in the crude drug, might be included in the next edition, in order to establish uniformity in the market supplies of this fluid extract. The following method has yielded excellent results for purposes of standardization:

Sample 10 Mils. Place on 10 Gms. of oak sawdust contained in a 6-inch evaporating dish. Mix well and allow to dry spontaneously for exactly six hours at room temperature, stirring occasionally. Place impregnated sawdust in a bottle. Add 100 Mils. of ether, which has been previously dried over anhydrous calcium chloride. Shake the bottle and contents for four hours. Filter off a 50 Mils. aliquot and place it in a 250 Mils. beaker, allowing the ether to evaporate spontaneously, and as soon as all the ether is off, place the beaker in a sulphuric acid desiccator and allow it to remain there for exactly 18 hours. Weigh. Then place the beaker in an oven at 110° C. until the weight is constant. The loss in weight during the heating represents "volatile extractive, soluble in ether."

A standard of not less than 8 Gms. of "volatile extractive, soluble in ether" per 100 Mils. of fluid extract would answer all standardization purposes.

The standard for crude drug is 10 per cent., but it is not practical to completely exhaust the drug.

*Fluid Extract Jalap.*—An assay process and standard for total resins might be included in the next edition in order to establish uniformity in market supplies of this product.

The following assay process, based upon the U. S. P. assay process for Jalap drug, has rendered excellent service:

Sample 10 Mils. Dilute with alcohol to 100 Mils. Place 20 Mils. of this dilution (corresponding to 2 Mils. of fluid extract) in a separator and proceed as in the assay of Jalap U. S. P.

As standard of 7 Gms. total resins per 100 Mils. can be recommended as being commercially obtainable, and representing the drug, Gm. per Mil.; the U. S. P. standard for the drug being 7 per cent. total resins.

*Fluid Extract Kola*.—Standardization is to be recommended for this product, so as to establish uniformity in market supplies.

The assay method for caffeine in Fluid Extract Guarana U. S. P. is also applicable to the assay of this fluid extract.

A standard of 0.9–1.1 Gms. caffeine per 100 Mils. is satisfactory, because it is based upon practical attainment and is familiar to the trade.

*Fluid Extracts Matico, Mezerium and Quercus*.—Deletion of these fluid extracts is suggested. The remarks under Fluid Extract Chirata also apply to these fluid extracts.

*Fluid Extract Sanguinaria*.—Standardization is to be recommended in order to establish uniformity in market supplies.

The following assay process has rendered excellent service for purposes of standardization:

Place exactly 5 Mils. of Fluid Extract Sanguinaria on 10 Gms. of oak sawdust. Allow to dry spontaneously in a warm place. Place the impregnated sawdust in a bottle. Add 100 Mils. of ether and 10 Mils. of 10 per cent. ammonia water. Shake the bottle and contents for four hours. Filter off an aliquot. Shake out with 1 per cent. sulphuric acid. Make acid extractions alkaline with 10 per cent. ammonia water and extract with ether. Evaporate ether extractions, dry residue at 80° C. and weigh as alkaloids.

Standard: 2.5 Gms. alkaloids per 100 Mils.

This standard is based on practical attainment, and the trade is perfectly familiar with fluid extract of this strength.

The assay process described above is the typical "immiscible solvent gravimetric alkaloidal assay" process. The only specific feature is the use of 1 per cent. sulphuric acid solution for extraction; weaker acid may be used, but 2 per cent. acid results in precipitation of alkaloidal sulphate which greatly interferes with drawing the acid extractions off from the separator.

#### SYRUPS.

*Syrup Iodotannin*.—An assay for iodine is desirable, because it is necessary to use heat in the preparation of this syrup, while the iodine is still in a free condition. A standard for iodine content will insure uniformity in market supplies of this syrup.



A satisfactory method of assay, which consists essentially of a modification of direct titration of iodides by *N*/10 silver nitrate and potassium sulphocyanide, is outlined in my "Laboratory Notes," on page 175 of the 1919 *Proceedings of the Annual Meeting of the Pennsylvania Pharmaceutical Association*.

#### TINCTURES.

TINCTURES FOR WHICH NO PRACTICAL CHEMICAL OR PHYSIOLOGIC METHODS OF STANDARDIZATION ARE AVAILABLE.

The remarks above under "fluid extracts for which no practical chemical or physiologic methods of standardization are available" also apply to these tinctures.

*Alcohol Percentages of N. F. Preparations.*—A list of alcohol percentages of N. F. preparations is desirable as being of assistance in preventing incompatibilities in manufacturing preparations and in compounding prescriptions.

The Revision Committee should experience no difficulty in obtaining satisfactory data for the establishment of these standards from the laboratories of pharmaceutical manufacturing companies which exercise scientific control of manufacture and also from other scientific sources.

#### TEST FOR HEAVY METALS.

The N. F., 4th edition, test for heavy metals makes no provision for those heavy metals beyond the lead and arsenic groups, principally zinc. The following modification is suggested:

Between the phrases "and again set aside for half an hour" and "The color produced, if any, etc.," add "evaporate to dryness. Redissolve residue in 1 Mil. of diluted hydrochloric acid, dilute with 10 Mils. of water, filter, make the filtrate alkaline with ammonia water, boil until nearly free from ammonia, filter, wash filter with enough distilled water to obtain 10 Mils. of filtrate, add 1 Mil. of ammonia water followed by distilled water q. s. 20 Mils. and saturate with H<sub>2</sub>S gas." Add the phrase "either by the hydrogen sulphide T. S. or the H<sub>2</sub>S gas," after "The color produced."

PHARMACEUTICAL RESEARCH LABORATORY,  
H. K. MULFORD COMPANY,  
PHILADELPHIA, PA.

## THE MANNA OF SCRIPTURE.\*

BY E. M. HOLMES, F.L.S.

The recent discussion in *The Chemist and Druggist* concerning the nature and origin of the manna of the Israelites has led me to venture to express the opinion of a botanist on the subject, for to a student of that science, especially to an economic botanist, the subject presents an exceedingly interesting problem.

The description given by the Jewish historian in the Pentateuch does not exactly fit in with any known vegetable production, and the various plants or plant products with which manna has been doubtfully identified from time to time cannot reasonably be considered by any botanist to meet the requirements of the case.

The plant that has most generally been accepted as being the manna of Scripture is a lichen, *Lecanora esculenta*, var. *mannifera*, Ehrenb., which is abundant on stones and rocks, and in certain stages of its growth is broken up by drought and violent winds into small particles, which collect in quantity under the lee of small bushes which arrest its career, or is carried away by rainstorms and deposited in wave-like furrows in sandy desert ground in considerable quantities. An illustration of this plant is given in Kerner and Oliver's "Natural History of Plants," Vol. I, p. 195, and a description of its curious growth and distribution in Vol. II, pp. 810, 811. Two other species are mentioned as being found mixed with it—viz., *Lecanora desertorum* and *Lecanora Jussufii*.

*Lecanora esculenta* is abundant from Persia and Asia Minor to Algeria and the Sahara in North Africa. But this lichen differs from manna in not appearing with the dew, not breeding worms and not stinking if kept for two days. I have had a specimen of it in my possession for over thirty years, and it is as hard and solid as when it first came into my possession. It is obvious, therefore, that it cannot be the manna of Scripture, as it does not possess any of its characters. It may be useful to quote here the actual descriptions given in the Pentateuch of the appearance of manna. The best account of it occurs in Exodus xvi, 14-36, which reads thus: "And when the dew was gone up, behold, upon the face of the wilderness a small round (or flake), small as the hoar frost upon the ground. . . . " Moses said, "Gather ye of it every man accord-

\* *The Chemist and Druggist*, January 3, 1920.

ing to his eatings;" and added, "Let no man leave of it till the morning." But some of them left it till the morning, and it bred worms and stank. When the sun waxed hot it melted. . . . "And the house of Israel called the name thereof 'Manna:' and it was like coriander seed, white; and the taste of it was like wafers made with honey."

The description given of it in Numbers xi, 7-9, is slightly different:

"The manna was like coriander seed and the eye thereof as the appearance of bdellium. The people went about and gathered it and ground it in mills or beat it in mortars and seethed it in pots and made cakes of it, and the taste thereof was as the taste of fresh oil. And when the dew fell upon the camp in the night the manna fell upon it."

It is obvious to any cryptogamic botanist that these characters belong to fungi rather than to lichens. Everyone familiar with British fungi knows how rapidly, even in our own temperate climate, many of the softer agarics become full of the grubs or larvae, of small flies or beetles, and how rapidly fungi grow when the conditions of warmth and moisture are suitable for their development. Melting in the sun (or as soon as the spores are mature) is a familiar phenomenon in our country in the case, for instance, of *Coprinus atramentarius*, which derives its specific name from the fact that the plant deliquesces into a black, inky fluid. The same genus also provides the edible species, *Coprinus comatus*. To mycologists, also, the gregarious character of many fungi is well known. I remember, some years ago, noticing on Saunton Sands, in North Devon, that apparently the ground was scattered all over in one place with what looked like bleached rabbit's dung, each nodule of which had a dark point in its centre, on stooping to take up one nodule to ascertain the cause of this appearance, it came up in my hand with a stalk of about six times its length, which had been immersed in the sand, and it proved to be the rare fungus *Tulostoma mammosum*. This may have some bearing on the statement that the eye or "appearance of manna was as the appearance of bdellium" (Numbers xi, 7), which may have indicated that the manna grains had a dark central spot.

The other substances which have been suggested as being the manna of Scripture are described in "Pharmacographia" (2nd ed.), pp. 414-416, and in Smith's "Dictionary of the Bible," 1865, p. 512; but these cannot possibly be regarded as answering to the

biblical description, since they are saccharine exudations from bushes or small trees, used when cleaned, like honey, to sweeten farinaceous cakes, but never made into cakes by themselves. Thus, although the tamarix manna, from *Tamarix Gallica*, var. *mannifera*, Ehrenb., is found in June, July and August, caused by the puncture of an insect, *Coccus manniparus*, Ehrenb., occurs in the peninsula of Sinai; the name manna (meaning, What is it?) would hardly have been applied to it by the Israelites when they could see its source. Indeed, the Arabs call it *Gazangabin*, meaning tamarisk honey, not manna. Moreover, these saccharine exudations do not breed worms and stink in two days, for specimens of them in the Hanbury Collection of Materia Medica, at 17 Bloomsbury Square have remained there unchanged for nearly forty years. When, therefore, soon after the publication of Mr. A. T. Swann's book on "Fighting the Slave-driver in Central Africa" appeared, I read his account of the manna that he saw on the plateau between the lakes Tanganyika and Nyasa, I recognized at once that the description he gives of it agrees almost word for word with the biblical account of manna, and I therefore wrote and asked Mr. Swann if he could, through any friends there, or travelers going to that region, obtain for me some of the plant, preserved in spirit or solution of corrosive sublimate, which presumably most medical missionaries take with them. In reply, he kindly promised to take the first opportunity that occurred to endeavor to get a specimen, but whether the opportunity never occurred or the promise slipped from his memory, I was unable to ascertain, since shortly afterwards I lost the memorandum of the name of the book and the author's name and address, and although I searched through a number of books on African travels I could not find the passage again until I saw a reference to it in the *C. & D.* in "Xrayser II's" note on manna a week or two ago, and now I cherish the hope that before my days are ended, I may yet be able to solve this riddle of the ages, or to see it solved by some other cryptogamic botanist; for I feel convinced that manna is a fungus hitherto undescribed and belonging possibly to a new genus. At all events, I intend to hang on to the trail I had lost until the enigma is solved. It may be interesting to quote here Mr. Swann's description of manna, word for word, for comparison with the biblical description already quoted (*loc. cit.*, p. 116):

"It was whilst passing through this district (the high plateau which separates the lakes Tanganyika and Nyasa), composed mostly

of sand stone and granite, and occupied by the Amambwi tribe, that I was shown a very curious white substance very similar to porridge. It was found early in the morning before the sun rose. On examination it was found to possess all the characteristics of the manna which is said to have fallen for the benefit of the Israelites. In appearance it resembled coriander seed, was white in color, like hoar frost, sweet to the taste, melted in the sun, and if kept overnight was full of worms in the morning. The natives were not allowed to gather it without asking permission from the chief. It required to be baked if you intended to keep it any length of time. This substance was seen some years afterwards in the same district by several Europeans now living (1910), who can vouch for the accuracy of my description of this food. When asked what it was and where it came from the natives replied, 'It's the food of God. No one knows where it comes from.' I have never seen or heard of it in any other part of the world, although it may be known to others. A cake of it was baked and sent to England, but no one appeared able to determine its identity. It looked as if it was deposited on the ground in the night, but in what manner I was never able to ascertain. No holes could be found in the ground near it or one might have concluded that insects unearthed it during the night. The only suggestion I could think of was that it might be a mushroom spawn, as on the spot where it melted tiny fungi sprung up the next night."

During the last few days I have had the privilege of conversing with a medical missionary, Dr. Wareham, who knows the district well where African manna was found; and he and Mrs. Wareham confirmed the statements made by Mr. Swann, but stated that they had only once seen the manna during eighteen years' residence in Africa. He has promised to endeavor to get some of the living manna preserved in spirit or formaldehyde or solution of corrosive sublimate, and to get some of the soil in which it grows sent separately in a small box. Mrs. Wareham suggested that possibly ants might have something to do with its appearance in such profusion. It is well known that in this country ants cultivate certain fungi in their nests, apparently for food when it is scarce outside.

The miracle respecting manna was undoubtedly its phenomenal production on an enormous scale in the immediate neighborhood of the Israelitish camp. In this respect it resembles other miracles related in Scripture, such as the multitude of fishes, the feeding of

the five thousand; but that the manna itself was a vegetable product, possibly of rare occurrence but miraculously increased in quantity, just as the quails were in this case driven by a particular wind, seems probable. That a plant occurring in Central Africa should also occur in Arabia is not at all improbable, since we know that plants often extend great distances along river basins, or occur on mountains at immense distances apart when the conditions are similar, although the plant may present slight variations, as in the Guide's Flower (*Leontopodium alpinum*), which occurs from Mont Blanc in the Swiss Alps to the Himalayas.

It is a remarkable fact that a deep valley runs for nearly 4000 miles from Arabia to the Cape of Good Hope, known as the Great Rift Valley, and along its sides there occur several forms of a plant of the genus *Acokanthera*, Nat. Ord. *Apocynaceae*, from one end of the valley to the other; *Acokanthera Deflersii* in Arabia, *A. Schimperi* in Northeast and Central Africa, and *A. spectabilis* and *A. venenata* in South Africa. It need not be surprising, therefore, if a cryptogamic plant like manna were found along the sides of this immense valley, extending from the Lebanons almost to the Cape of Good Hope, wherever the conditions were suitable for its development, since the spores of fungi are easily carried on the feet of birds. There is, therefore, apparently no reason why the manna of Tanganyika should not be identical with that of Arabia. Gregory, in "The Great Rift Valley" (p. 5), states that a series of thirty lakes occur along its course, only one of which communicates with the sea, thus indicating that it was an ancient river bed, and giving some support to the theory that this was the bed of the ancient river Gihon (Genesis ii, 13), which "compasseth the whole land of Cush." The land of Cush, according to Smith's "Dictionary of the Bible" (1865, p. 223), evidently included both Arabia and the country south of the western coast of the Red Sea.

According to Gregory ("The Great Rift Valley," p. 51), the Arabs told him that the Red Sea is simply water that did not dry up after Noah's deluge; and the Somali say that when their ancestors crossed from Arabia to Africa there was a land communication between the two across the Straits of Babel Mendeb. There is geological evidence to show that great earth movements have happened along the Great Rift Valley at a recent geological date. There seems to be nothing improbable, therefore, in the possible occurrence of the scriptural manna plant in Central Africa as well as in Arabia.

But there are one or two features in the biblical description of manna that call for comment. One is the reason why it kept over the Sabbath without becoming filled with worms and stinking. The directions given to bake or seethe it would naturally kill all insect life in it; and the manna, that was to be preserved for generations as evidence of the Israelites being miraculously fed, was probably baked, and may have become hard or horny in the process. It is not easy to explain otherwise why they "ground it in mills or beat it in mortars," especially as in the fresh state it was soft enough to melt in the sun's heat. The text is difficult to follow, but in Numbers xi, 8, it seems to imply that, after grinding it, it was seethed and made into cakes.

The fact that the manna was abundant enough to feed a multitude of people for forty years indicates that by some unrecognized means the plant miraculously increased, and the conditions were those of uncultivated land, since it ceased when they "came to land inhabited," "in the borders of the land of Canaan."

Another point is the continuous production of the plant for forty years and all the year around. But we have the evidence at home that the mushroom, which in the wild state is usually confined to August and September, can be produced all the year round if the natural conditions of heat, moisture and food are artificially provided. There may have been conditions connected with the manner of life of the people which produced artificially the requirements of the plant. At all events, the study of the life-history of the manna plant in the future offers many interesting problems to the research workers at Khartoum, or elsewhere, if the plant can be obtained and cultivated.

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#### NOTE ON THE DE-ARSENICATION OF SULPHURIC ACID BY HYDROGEN SULPHIDE.\*

BY T. S. MOORE.

According to the published information, the strength of sulphuric acid submitted to de-arsenication by hydrogen sulphide must not exceed 110° Tw. (64.26 per cent.  $\text{H}_2\text{SO}_4$ ), and in many works much less than this, down to 100° Tw. (59.7 per cent.  $\text{H}_2\text{SO}_4$ ). The ex-

\* From *Jour. Soc. Chem. Ind.*, December 15, 1919.

periments described in this paper were undertaken at a time when the demand for arsenic-free C. O. V. was very large and when all unnecessary concentration had to be avoided on account of shortage of plant, to find out whether more concentrated acid, particularly Glover tower acid of about  $174^{\circ}$  Tw. (80 per cent.  $\text{H}_2\text{SO}_4$ ) could be de-arsenicated without prohibitive loss of sulphuric acid by reduction.

The experiments were carried out at the temperature of the laboratory. Hydrogen sulphide at the rate of one bubble a second was passed through 200 Gms. of the acid under examination, and the product filtered through asbestos in three separate portions: (1) Without any special precaution, (2) with hydrogen sulphide passing through the liquid while filtering, and (3) without precaution, after the liquid and precipitated arsenious sulphide had remained together for one or two days.

In de-arsenicating arsenical C. O. V. (95 per cent.  $\text{H}_2\text{SO}_4$ , 0.15 per cent.  $\text{As}_2\text{O}_3$ , 0.11 per cent.  $\text{As}_2\text{O}_5$ ) it was found (1) that the process was slow, taking  $2\frac{1}{2}$  hours in laboratory apparatus; (2) that excessive reduction of sulphuric acid occurred, the strength of the resulting acid being 91.8 per cent.; (3) that if filtration from the arsenic trisulphide is carried out immediately after the precipitation the arsenic content is 2 to 3 parts  $\text{As}_2\text{O}_3$  per million, but that the arsenic content is higher the longer the filtration is delayed; and (4) that if hydrogen sulphide is passed through the liquid during filtration the arsenic content falls to less than 1 part  $\text{As}_2\text{O}_3$  per million. Further, under the conditions last mentioned, the acid coming through the filter is perfectly clear, but soon becomes cloudy owing to the precipitation of sulphur, which shows that the rate of oxidation of hydrogen sulphide by strong sulphuric acid is not large enough to prevent the accumulation in solution of an appreciable quantity of the gas.

With arsenical C. O. V. diluted to contain approximately 80 per cent. of sulphuric acid it was found: (1) That the rate of reduction of the sulphuric acid is quite small (original acid contained 79.7 per cent  $\text{H}_2\text{SO}_4$ . After one hour's treatment with hydrogen sulphide, the acid contained 79.4 per cent.  $\text{H}_2\text{SO}_4$ . After two hours' treatment it contained 77.8%  $\text{H}_2\text{SO}_4$ ); (2) that acid filtered immediately after one hour's treatment contained 1 part  $\text{As}_2\text{O}_3$  per million, and the arsenic content was not diminished by passing hydrogen sulphide during filtration; (3) that when filtration was delayed



the arsenic content had risen only to 1.5 parts  $\text{As}_2\text{O}_3$  per million. Two days after the acid has been filtered it still smells of hydrogen sulphide, which shows that the rate of reaction between hydrogen sulphide and 80 per cent. sulphuric acid is small.

The behavior of 70 per cent. acid resembles that of 80 per cent., the chief differences being that (1) de-arsenication is slightly more rapid, (2) filtration of the arsenic trisulphide may be delayed several days without any serious increase of the arsenic content, and (3) there is even less reduction of sulphuric acid.

Finally, an experiment with Glover tower acid of unusually high arsenic content was carried out, in which hydrogen sulphide in fine bubbles was passed through 500 Gms. of the acid contained in a bottle fixed on a shaking machine. One hour's treatment with hydrogen sulphide proved insufficient for this acid, and in a second experiment treatment was continued for  $1\frac{3}{4}$  hours. Part of the product was filtered immediately and part after two days. The results of analysis were:

	Before Treatment. %.	After Immediate Filtration. %.	After Standing Two Days. %.
$\text{H}_2\text{SO}_4$ .....	77.1	77.1	77.1
$\text{N}_2\text{O}_3$ .....	0.18	None	None
$\text{As}_2\text{O}_3$ .....	0.29	Between 0.6 and 1 part in $10^6$	
$\text{As}_2\text{O}_5$ .....	1.58	None	None

These figures need some comment, for as they stand they give the impression that there is no loss of sulphuric acid. The following calculation shows that de-arsenication should actually cause an increase of the sulphuric acid content. The reactions proceeding are:



Thus, apart from absorption of water from the atmosphere and from reduction of sulphuric acid, 100 Gms. of the original acid containing:

77.1 Gms.  $\text{H}_2\text{SO}_4$   
0.18 Gm.  $\text{N}_2\text{O}_3$   
0.29 Gm.  $\text{As}_2\text{O}_3$   
1.58 Gms.  $\text{As}_2\text{O}_5$   
20.85 Gms.  $\text{H}_2\text{O}$

should give  
with  $\text{H}_2\text{S}$

77.1 Gms.  $\text{H}_2\text{SO}_4$   
0.05 Gm.  $\text{H}_2\text{O}$   
0.08 Gm.  $\text{H}_2\text{O}$   
0.63 Gm.  $\text{H}_2\text{O}$   
20.85 Gms.  $\text{H}_2\text{O}$

i. e., 100 Gms. of acid should become 98.71 Gms. after de-arsenication, so that the strength of the sulphuric acid in the de-arsenicated product should be  $\frac{100 \times 77.1}{98.71} = 78.1$  per cent. Since it was found to be 77.1, there is an apparent loss of 1.3 per cent. of the sulphuric acid originally present. This figure cannot be taken as accurate, for absorption of water may have occurred, and, further, it is not possible in small experiments to estimate the yield of de-arsenicated acid at all exactly. But it can be taken that the loss of sulphuric acid by reduction is less than 1.3 per cent. of the original sulphuric acid. The loss could certainly be diminished by (a) using a more efficient apparatus for mixing the gas with the acid, (b) stopping the treatment before the de-arsenication had gone so far as the point reached in the experiment, and (c) using a Glover tower acid of more normal arsenic content, for all these conditions would diminish the duration of treatment.

From these experiments it is clear that for practically complete de-arsenication of acid of any strength up to 95 per cent. the only essential condition is that the acid after treatment must contain dissolved hydrogen sulphide, and so long as this condition is fulfilled the acid can stand in contact with the arsenious sulphide without any serious increase of arsenic content. As soon as the hydrogen sulphide has been destroyed the acid takes up arsenic again at a rate depending upon its strength.

E. Schmidt (*Arch. Pharm.*, 45: 255, 1917) states that although water, alcohol, and dilute solutions of hydrochloric acid cause appreciable decomposition of arsenious sulphide, such decomposition is prevented by the presence of small quantities of hydrogen sulphide. The above experiments shows that hydrogen sulphide has a similar effect, even in the presence of strong sulphuric acid. —Royal Holloway College (University of London).

## MEDICINAL PLANTS IN BAHIA.\*

BY CONSUL EDWARD HIGGINS,

BAHIA, BRAZIL, NOV. 1, 1919.

The State of Bahia, Brazil, offers to the medical world an abundant and varied supply of plants, roots, barks and gums, including many

\* From *Commerce Reports*, Dec. 26, 1919.

of recognized value and some regular articles of export, such as ipecacuanha root, araroba powder, jaborandi leaves, and Jatoba gum. Most of the plants exist in practically inexhaustible quantities; but orders must be placed in advance with local exporters, for there is no regular trade even in those now figuring among the State's exports. The supply depends entirely upon the demand. There follows a list of the most important medicinal plants found at convenient distances from the city of Bahia:

*Angelica* (*Gentiana rubra*).—Aromatic, antiseptic and antispasmodic; a powerful remedy against intermittent fevers.

*Arco leaves*.—A substitute for the coca leaves of Peru; a stimulating and powerful tonic, yielding cocaine.

*Araroba or Goa Powder*.—This is a powder taken from the heartwood of a tree known locally as "armagoso do matto" (*Vouacapoua araroba*), which contains a substance known as chrysarobin, used in the treatment of skin diseases.

*Barbatimao Bark*.—The inner bark contains phosphate of lime, tannin and an alkaloid similar to quinine; it is a sedative, and reduced to powder makes an excellent dentifrice.

*Cajueiro* (*Anacardium occidentale*).—The bark is astringent and is an efficacious remedy against diabetes.

*Caroba leaves*.—Antisymphilitic and antibubonic; well known in Brazil as a powerful blood cleaner, used externally and internally. It is a vegetable mercury and is said to be superior to sarsaparilla and other blood purifiers.

*Cambará Leaves*.—A strong sedative and expectorant, for bronchitis, coughs and pulmonary ailments.

*Cameleao da costa*.—Remedy for stomach trouble.

*Cestrum Leaves*.—A strong narcotic, said to be poisonous, also used in baths against hemorrhoids, a powerful insecticide. The damp leaves are applied to wounds, first inflaming them, but afterwards cleaning and healing them.

*Congonha*.—A stimulant, diuretic as a tea.

*Gervao*.—One of the best disobstruents known, aids digestion and eases laborious births.

*Imbauba*.—Remedy against coughs, bronchitis and asthma.

*Imburana*.—Inner bark contains coumarin; it is aromatic, an expectorant and a stimulant.

*Ipecacuanha*.—This is a shrub growing in the shade of the forest, the root of which is dried and powdered for use in medicine. It is valued as an expectorant, diaphoretic and emetic. It is not cultivated, but care is taken in digging up the plants to leave sufficient roots in the soil for another crop.

*Jaborandi Leaves*.—Aphrodisiac, sudorific and stimulating. From these leaves is extracted pilocarpine, which is used in tonic preparations for the hair.

*Jurubeba* (*Solanum paniculatum*).—Remedy for congestion and maladies of the liver.

*Loco Leaf*.—A vegetable caustic.

*Carnauba Wax*.—A tasteless, aseptic wax extracted from the leaf of a palm tree known locally as the “carnaubeira” and employed in the preparation of ointments, pomades and pills.

*Mamona*.—This is Portuguese for the castor plant, which was introduced into Brazil from India and China by the earlier colonists, but spread so quickly as to have the appearance to-day of a forest plant. Both the seed and oil are exported from Bahia in increasing quantities each year.

*Manaca Root*.—Antisyphilitic vegetable mercury.

*Jatobá Gum*.—Jatobá is a name applied to several species of trees found in the valley of the River Sao Francisco, which traverses the northern and western parts of the State of Bahia. The gum which is extracted from this tree is employed in the composition of syrups for pulmonary affections. It is variously known, locally, as jatobá, jatahy and jutahy.

*Jatobá Bark*.—The bark of the above-mentioned tree is also of value in the preparation of medicines and is employed as an astringent and carminative.

*Mango Tree* (*Mangifera indica*).—The leaves are antiasthmatic.

*Menstrasto*.—A plant, stimulating against colics and used in fevers, also in baths to cure weakness.

*Milhomens* (*Aristolochia cymbifera*).—Used against paralysis, dropsy and stomach trouble.

*Mulungu* (*Erythrina mulungu*).—The inner bark is a powerful sedative, narcotic and antispasmodic, and is a substitute for belladonna; it also exercises a special action on the liver; in doses of 5 centigrams it will induce sleep.

*Pareira Brava Root* (*Cissampellos pareira*).—A powerful tonic, remedy for stomach trouble, bladder trouble, beri-beri, brain fever and meningitis.

*Pao ferro*.—A bark used against diabetes; the seeds furnish a strong tonic and diuretic.

*Purga de campo*.—Remedy for fevers, pleurisy, tumors and cancerous wounds.

*Pindahiba*.—Remedy for stomach trouble and for intestinal flatulence.

*Quina-quina*.—A bark used against fevers.

*Quitoco*.—Carminative, antihysterical and digestive; used in baths for muscular pains in the body.

*Samambaia*.—Used for rheumatism.

*Velame de campo*.—Blood cleanser, antisyphilitic and anti-rheumatic, for skin diseases and swelling of the glands.

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## NOTES ON THE GINGER-BEER PLANT.\*

By E. M. HOLMES, F.L.S.

Although this curious substance has been used for many years, both in this country and the United States, its original source appears to be unknown, and the names which are popularly given to it indicate a desire to keep its origin and nature a secret. Among the most far-fetched of the names under which specimens have been sent to me with inquiries as to its nature is "Balm of Gilead!"

Evidently the scientific examination of this substance by the late Dr. H. Marshall Ward, published in the *Proceedings of the Royal Society* as long ago as 1891 (Vol. 50, pp. 261-265), and

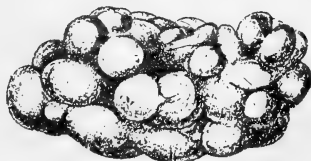


FIG. 1.—The Ginger-Beer Plant.

further elaborated in a second paper, published in the *Philosophical Transactions* of the same society in 1892 (p. 125), have been over-

\* *The Pharmaceutical Jour. and Pharmacist*, Jan. 3, 1920.

looked by busy pharmacists, but the brief summary of Dr. Marshall Ward's researches given by Prof. Reynolds Green in his work on "Fermentation" (p. 321) should not have escaped notice, except for the fact that Prof. Green did not provide an alphabetical index to his otherwise excellent publication. The same fault applies to Salter's translation of D. L. Lafar's "Technical Mycology," in which, on pp. 256-267, illustrations of the two chief constituents of the ginger-beer plant are taken from Dr. Marshall Ward's paper. Both these two last-named works are in the library of the Pharmaceutical Society.

It may, however, serve a useful purpose if a summary of all that is at present known concerning the life-history of the ginger-beer plant be placed on record in the pages of the JOURNAL for future reference.

In appearance the ginger-beer plant bears some resemblance to pearl-barley that has been boiled, but the nodules vary in size from that of a pinhead to nearly an inch in diameter (see Fig. 1). It belongs to a class of symbiotic ferments in which a yeast and a bacterium live together, the one assisting in and promoting the work of the other. To this class belong also kephir, the ferment of koumiss, and a ferment found on the sugar cane in Madagascar. The first is used in the fermentation of cow's milk in the Caucasus, and the second in the fermentation of mare's milk in the steppes of South-west Siberia. The ginger-beer plant and the Madagascar ferment can ferment saccharose, maltose, glucose and fructose, but not lactose. In this particular feature they differ from the kephir and koumiss ferments, which can split up lactose. Kephir and the Madagascar ferment both have a similar appearance to the ginger-beer plant, but the koumiss ferment is not used in a separate state, a portion of fermented milk being added to some fresh milk when required. The products of fermentation are chiefly alcohol, carbonic acid and some lactic and acetic acids, and in the case of the Madagascar ferment some succinic acid, the acetic acid being formed directly from the sugar, and not through the medium of the alcohol.

When a few pieces of the ginger-beer plant are put in a 10-30 per cent. solution of cane sugar and the bottle put in a warm place fermentation takes place in about twenty-four hours and the liquid is then observed to become turbid, and bubbles of gas begin to ascend. This turbidity is due almost entirely to the yeast-cells which are shed from the nodules of the plant, which rise and fall

in the liquid and multiply in it, and form a grayish deposit at the bottom. The liquid becomes charged with carbon dioxide, and becomes more or less viscous, so that the gas-bubbles rise more slowly. This viscosity is due to the swollen or vermiform bacteria which become distributed throughout the liquid, which becomes acid as well as viscous. The chief products of the fermentation of the ginger-beer plant are carbonic and lactic acid, with traces of alcohol and acetic acid.

With regard to the constituents of the symbiotic ferment known as the ginger-beer plant, Dr. H. Marshall Ward found that it consisted chiefly of two plants, the one a yeast (*Saccharomyces pyriformis*) and a hitherto undescribed bacterium, to which he gave the name of *Bacterium vermiforme*, from its worm-like appearance under the microscope. The appearance of these two plants is shown in illustration 2 here given, taken from Dr. Ward's second paper, in the *Philosophical Transactions of the Royal Society* (p. 1251). The oval cells in Fig. 2 are those of the yeast *Saccharomyces pyriformis*, entangled in the worm-like filaments of the *Bacterium vermiforme*. These—which form the chief bulk of the ferment—are the two essential constituents in it, since Dr. Ward found

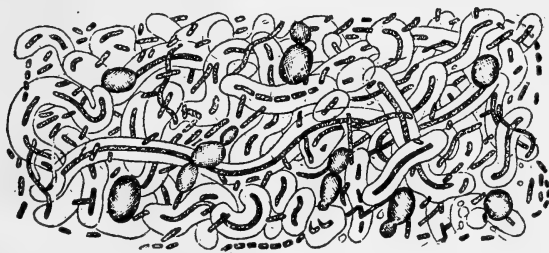


FIG. 2.—The Symbiotic Condition.

that it was possible, under proper conditions, to reconstruct the plant from pure cultures of these two plants isolated from a fermenting liquid. The bacterium filaments are generally much coiled and twisted together, sometimes broken into short rodlets, or even cocci, arranged in chains. The separate filaments are surrounded to a greater or less extent by a pellucid gelatinous sheath, and it is to this that the consistency of the ginger-beer plant is due. The sheath consists of the greatly swollen layers of the cell membrane, which may be developed on one side only or along part of its length, or may even be absent altogether. The branched form appears

to be due to a persistent one-sided development of these layers. The bacterium itself, as distinct from the sheath, measures about  $0.5\ \mu$  in diameter, and varies from  $0.5\ \mu$  to  $5.0\ \mu$  in length, the sheath being often ten times the diameter of the cell. These thickened walls occur in many of the Nostocaceae, especially in the Oscillatoriae. The ginger-beer plant can be dried and shrunk up into a horny mass, in which condition it can be stored for future use.

Mr. E. R. Nichols, of Middlesbrough, who recently sent me a specimen, writes that it is largely used in that district in preparing a drink called a wine. For this purpose 4 ounces of sugar and 4 ounces of treacle are mixed with  $1\frac{1}{2}$  pints of warm water to form the mother liquor. Small pieces of the plant are then added, and the mixture is kept in a warm place. Each day about a teaspoonful of sugar is added. There is brisk fermentation, and a palatable drink is soon ready. The ferment quickly increases, and can be used to prepare a fresh batch.

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## THE TEACHING OF THERAPEUTICS.\*

BY HOBART AMORY HARE, M.D.,

PROFESSOR OF THERAPEUTICS, MATERIA MEDICA AND DIAGNOSIS, JEFFERSON  
MEDICAL COLLEGE, PHILADELPHIA, PA.

I am writing this paper because I am hopeful that it may direct attention to what is a crying fault in medical education to-day, namely, the neglect of teaching students how to treat patients for the alleviation or cure of disease. I am hopeful that some good may come of it because the Council on Pharmacy and Chemistry of the American Medical Association for years past has been endeavoring to inform physicians regarding the use of proprietary products and to persuade them to prescribe drugs, proprietary or not, intelligently.

The work that the Council had done is, of course, praiseworthy in intent, and is good as far as it goes in one line, to wit, to improve medical practice among graduates; but the prime difficulty lies in the teaching of practical therapeutics to the undergraduate and to the hospital intern. This embryo practitioner in almost every medi-

\* Reprinted from *Jour. American Medical Association*, Feb. 7, 1920.



cal school has no training in pharmacy, little or no training in the use of the official names of drugs or of their doses, and no training whatever in the fact that doses of different sizes, although they be of one drug, may be useless, useful or harmful, or become so after some days. He, therefore enters practice utterly at sea when he is called on to write a prescription.

I have known of eye drops to be ordered by the quart, oleoresins mixed with aqueous solutions, powerful alkaloids, such as strychnine, put in a mixture with potassium iodide, whereby nearly all the strychnine went into the last dose, and a host of other errors too numerous to mention. I have seen a thousandth of a grain of arsenous oxide given three times a day to an adult, and a grain of atropine put in each pill; and no druggist exists who, if diplomacy did not restrain him, could not humiliate almost every physician whose recipes come to his shop. Because the medical man knows nothing of the bulk of drugs or the most efficient vehicles, or excipients, he takes the easiest way out of his dilemma and orders products already prepared, which products are often the result of much experience and scientific pharmacy.

The remedy for all this is to have every student make in a pharmacy laboratory at least one representative of each class of preparations official in the Pharmacopoeia and the National Formulary. I believe that this is done in only one school of medicine in the United States.

The young graduate, having had no experience or teaching as to doses, naturally used doses that some commercial laboratory names. He may have been taught "doses," but he has no idea that small doses of digitalis may be useful in one case, whereas almost toxic doses may be absolutely essential in another, and so loses the patient that needed the large dose. He uses the compound mixture of licorice as a vehicle in a case of profuse bronchorrhea or threatened pulmonary edema, not knowing, or forgetting, that its most active ingredient is antimony, which is absolutely contraindicated.

When he becomes an intern in a hospital, he learns one thing of great importance, namely, that the chiefs who prescribe little and "let the patient get well" often obtain the best results; or if he is on a surgical service, the entire drug therapy may be in his hands, and the chief often boasts that he "knows nothing about drugs and don't want to." On the medical side in large hospitals he will find a hospital formulary from which mixtures are made up by the gallon

with all sorts of drugs, and contradictions, with widely varying doses of the ingredients; but there is a standard dose of the whole mess whether it be for a young girl of 16 weighing 100 pounds or an old rounder weighing 200 pounds. Not only this, but these mixtures go by names which often do not mention the most active ingredient, or, worse still, go by numbers, so that the order on the treatment card reads: "No. 23, dessert-spoonful t. i. d."

The fault does not stop with internship. Never having been taught practical therapeutics, the man steps into practice a fair mark for the loquacious traveling salesman who places him in the vocative by being familiar with what he ought to know. Some years ago, telling a distinguished ex-president of the Association that a patient was getting acetphenetidin, I found he did not know it was phenacetin. When he was told that the first term was the official one, he laughed and admitted that he had asked a student what he would use in a given case, and the reply was "phenol." The clinician "long" on pathology but "short" on therapeutics then informed the astonished youth that "phenol was no doubt very good, but carbolic acid was better."

*Proper Method of Training the Student.*—The remedy for the state of affairs just described is in teaching and experience when a student. This, in my experience, which is a fairly large one, is best accomplished by having the student, in his course, not only taught doses by rule of thumb, but also given the opportunity to prescribe for suppositive or actual cases, and to see the results of his order, both as to the prescription itself and as to its effect on the patient. Under the direction of an assistant professor the whole class may attend a therapeutic conference, or quiz, on the treatment of a given class of diseases, and during the conference several of the men who advise plans of treatment are called to the blackboard to put in black and white what they have suggested. When they have finished, the instructor, who has continued his quiz in the meantime, criticizes the pharmacy, the doses, the form, the combinations, the therapeutics and the quantity in the whole prescription, as well as the Latin.

The number of occasions on which such criticisms lead to howls of delight at the discomfort of the man at the blackboard may be subversive of discipline, but all hands remember how John Jones wrote for nitrohydrochloric acid, iodide of potassium, tincture of

gentian and tincture of iron in a quart of water, particularly if the mixture is prepared forthwith.

This large class teaching is driven home by a junior teacher taking the class in sections and having it spend one or two hours a week for several weeks writing prescriptions, for suppositive cases, which are then criticized, and the writer asked to give his reasons for using each remedy.

The regular medical ward classes should emphasize therapeutics; and, in addition, clinical, not laboratory, pharmacology should be taught. This is done by demonstrating a case of auricular fibrillation both at the bedside and with the electrocardiograph, and then giving full doses of digitalis, a second demonstration revealing the effects. So, too, the mode of action of atropine in partial or complete heart block is demonstrated, and the effects of nitrites in lowering pressure are taught by seeing a patient to-day with high pressure and again at the next visit with a reduced pressure. Any number of these therapeutic demonstrations can be made by the regular ward class teacher, and made still more useful if a demonstrator of clinical pharmacology who can use the polygraph and electrocardiograph is given proper hours. By this means the student is taught how drugs act and how various doses act, entirely apart from the didactic lectures on therapeutics or the general therapeutic clinics given by the head of the department, who deals of necessity with principles and practice.

*Faults in Present Methods.*—All this seems so obviously practical that the question arises, "Why is it not done?"

The answer is that there is not time. If there is not, why not? There is not time for two chief reasons. The first is that the student is taught too much of the special art of the specialties, many of which he will never attempt to practice; and unless he takes a post-graduate course after several years in general practice, he ought not to try to practice. At present the young graduate can talk learnedly of the difference between paralytic and concomitant squint or about the Bárány test, but is stumped when told to write a recipe for diarrhoea.

The second reason is that the laboratory of pharmacology has drowned practical therapeutics, and has done it so effectively that in most schools literally no bedside therapeutics as a separate branch is taught, the original chair of therapeutics being filled by a lab-

oratory pharmacologist who in some instances is not even a doctor of medicine, or if he has the degree of M.D. has never practiced a day in his life or even been an intern in a hospital. When he attempts to tell students bedside facts, it is as if he were an astronomer trying to teach a sailor how to navigate a ship without ever having been to sea. As he lacks bedside experience, he teaches, for example, that the best treatment of fever is a combination of the cold bath and coal-tar antipyretics, when every one who practices knows that this is a great error. It is enough to bring the gray hairs of Dr. Simon Baruch, the great apostle of hydrotherapy, in sorrow to the grave, and if carried out will bring many patients there.

Valuable time which should be spent at the bedside learning how to use drugs is employed in having students carry out pharmacologic technic in a course of six or eight weeks or their equivalent. It is safe to say that not one man in a thousand who takes this course becomes a pharmacologist or learns to be an efficient technician. What the student needs is not to do the experiments himself but to see them done by a man so well trained that results are produced that make a demonstration that really demonstrates the fact to be remembered. I can see no more reason for making a group of students, designed to be practitioners, make bungling experiments with a Kronecker-Bowditch heart apparatus than I can for their performing amputations and visceral operations on dogs or cats with the idea that they will become good surgeons; indeed, there is less reason. One cannot make a man who has no music in his soul a violinist in a six weeks' course, and probably it is safe to say that the majority of excellent physicians have not the qualities which produce original contributions to medical knowledge.

*Need for the Teaching of Practical Therapeutics.*—To quote Sir George Makins,<sup>1</sup> in an address to the Medical Society of Manchester:

"A survey of these considerations should exert a definite influence upon the determination of the nature of the course of education best suited to the development of the doctor upon whose efficiency the happiness and health of the nation so largely depends. It is clear that for the great bulk of the profession a path must be found by which advances in science are utilized for the perfection of the art of medicine, but it cannot be possible to elevate every medical man to the position of an apostle of pure science. . . ."

<sup>1</sup> Makins, *Brit. Med. J.*, 2: 590 (Nov. 8), 1919.

"All men are not endowed with a truly scientific spirit; the power of evolving great principles is reserved to the few, and even the correct appreciation and application of those which have been laid down is not a faculty universally enjoyed. Again, the power of reasoning, the possession of initiative and invention, and the facility of developing technical skill, are qualities very unevenly distributed among the class of man who adopts medicine as his profession. The reasons which lead to his choice are by no means always governed by the degree of aptitude he possesses for the calling he decides to follow. To some the science of medicine appeals; some adopt medicine from the lofty motive of desiring to benefit mankind; some boys are born to succeed to a family practice; some become students of medicine because the choice coincides with that of a friend; in some business capacity is nil; in others it is the mainspring of the future career and dominates all other feelings or aspirations. Lastly, in not a few instances the initial choice has never been made the subject of serious thought or consideration."

My point is not that there should not be teachers of pharmacology. On the contrary, there should be, because it is only by the efforts of these men that the scientific or investigative side of therapeutics can be advanced and the errors of empiricism corrected. Their existence develops those who have the talent, initiative, the proper deduction and the love of investigation, and their methods of thought and mode of study are examples of the highest type of medical man; but in their enthusiasm they should not forget that 999 of their pupils want to know how to make the sick well and do not want to know by personal experiments on dogs the effect, for example, of cutting the animal's sympathetic nerve, or the action of cocaine on the eye. If this is to be taught, let the pharmacologist make the experiment and demonstrate the result.

It may be said that I do not know whereof I speak; but I do, for I was once a pharmacologist myself. In the eighties I worked in laboratory pharmacology, and taught it, too, as a somewhat long list of titles in the Index Catalogue will show. I am not an iconoclast, and no one rejoices more than I do that the only pharmacologic laboratory in the United States in 1886 has been followed by two score of such laboratories from which a wealth of wonderful work was originated; but it is *postgraduate work*. I am pleading that hours now used otherwise may be employed to teach not only the theory but also the practice of therapeutics. When this is done, the work of

the Council on Pharmacy and Chemistry will be helped in its completion; for, when the practitioner knows how to prescribe, he will not tolerate the commercial concern that poses as his teacher.

The closing paragraph of a recent editorial<sup>2</sup> has a bearing on this subject. I have substituted the word "pharmacologist" for "physiologist," and "pharmacology" for "physiology."

"It is quite possible that, as has been suggested, we are approaching the time when there will be two types of persons connected with each clinical department, namely, the clinical pharmacologist, whose chief work will be the intensive study of selected groups of cases and the instruction of students in the application of the principles of pharmacology to the elucidation of disease, and the clinician, whose chief function will be the care of the patient and the instruction of the student in the practical methods of diagnosis and treatment. Obviously, some arrangement already exists in some of our better schools. In institutions in which full time medicine has been introduced, there has been a distinct effort to appoint as heads of the clinical departments men of the investigative type. One question that Addis' discussion raises is whether in our enthusiasm for laboratory research we have not overlooked the importance of purely clinical investigation and of the type of physician that naturally tends toward this."

At present an attempt is made to make pharmacologists out of men who are going to practice medicine. A real pharmacologist is a highly educated man in physiology and chemistry, an investigator, a discoverer, and by rights a leader in the higher realms of therapeutics—one who should teach medical students how drugs can be studied and should be studied in the laboratory, and to determine fundamental facts about remedies. But to try to train the general run of students, who will never have a laboratory, to be pharmacologists without first teaching elementary practical therapeutics, is somewhat like a great opera singer trying to make every one a great singer, or as if one should attempt to make his infant son sing before he tried to teach him to walk. The use of instruments of precision necessary for the study of drugs, if taught at all, should be at the bedside. I repeat what I said above: "The lack of training as to what to do, what not to do, and when to do, as to remedies, is one of the weak spots in medicine to-day." I firmly believe that

<sup>2</sup> "The Teaching of Clinical Medicine," editorial, *J. A. M. A.*, 74: 35 (Jan. 3), 1920.

if the present generation of students is properly taught practical therapeutics, the chief labor of the Council on Pharmacy and Chemistry will be an accomplished fact, for the right way will be the easiest way. Let us first make good physicians and from these may be sifted out those who can and want to become laboratory pharmacologists.

## THE TRAINING OF PHARMACEUTICAL CHEMISTS.\*

The sale of drugs and poisons is limited in most countries to certain persons. These persons become qualified for registration as pharmacists or pharmaceutical chemists after receiving a special training. In the various States of the Commonwealth of Australia the pharmaceutical student must reach a minimal standard of general education which is laid down by regulation. The student serves as an apprentice to a registered pharmacist for a number of years, whereby a knowledge is obtained of the practice of the profession. The student has sufficient opportunity of gaining acquaintance with his duties to render him proficient in the routine work of preparing drugs for medicinal use. This period is long enough to form habits of accuracy and attention, so that there will be little fear of mistakes occurring in the prepared medicines. In addition, the student attends courses of systematic instruction in botany, chemistry and *materia medica* at some college or university where these subjects are taught in an approved manner. The student acquires a knowledge of the various parts of vegetable substances and of the characteristic features of the plants from which the medicinal substances are derived. He is taught the chemistry of the principal inorganic and organic bodies, the outlines of qualitative analysis and the methods used for the quantitative estimation of the substances used as drugs. Above all, he is made familiar with the appearance of drugs, with their characters and with the tests to which they respond. Before registration the student has to satisfy examiners that he has attained proficiency in the subjects of study. At the termination of the period of instruction the pharmacist is able to recognize with ease the nature of the drugs with which he deals. In some States the student also re-

\* From *Med. Jour. of Australia*; through *The Australasian Jour. of Pharm.*, Nov. 20, 1919.

ceives systematic instruction in respect to the preparation of drugs for administration.

Many drugs act in a potent manner on the functions of the body. If they are given in too large dose they behave as poisons and may lead to death. Their use depends upon their administration in exact quantity. The training of the pharmacist is designed to make him precise in his measurements and trustworthy in his use of drugs. The reliability of the pharmacist is dependent to a considerable extent on his ready knowledge of the appearance and characters of drugs and their preparations. This knowledge guarantees the accuracy of his dispensing practice.

The restriction of the retail sale of drugs to these trained persons has for its aim the preservation of the public against errors in the purchase of drugs. The nature of drugs is such that the purchaser must be protected as far as possible from mistake in respect to the article that has been bought. *Caveat emptor* has no application to the purchase of medicines. The qualities of drugs are in many instances laid down in a pharmacopoeia operative in the particular country. The pharmacist endeavors to ascertain that the drugs he sells are of the necessary purity. Persons who buy drugs from those who are not registered pharmacists, do so at their own risk. They make no use of those safeguards which have been laid down for their protection. They must abide by the consequences of their act. When the purchase is made from a registered pharmacist, the buyer has a right to receive an article of the nature that he demands. The pharmacist is bound to use reasonable care in obtaining drugs and in dispensing them. On him rests the responsibility of making sure that he uses pure drugs and that these are measured in an accurate manner. In return the public owes to him the duty of seeing that his trade is not invaded by untrained persons with no specific knowledge of drugs and their use.

Accidents will happen. There are no means by which they can be completely abolished as long as powerful poisons are used as drugs. They will be less frequent when the dispenser is aware of the accumulated experience of the ages in the methods of guarding against them. They will be diminished in number with increased knowledge of the behavior of particular drugs under different circumstances. In this case, knowledge may mean power to avert the consequences of an error that has been already made.



## BOTULISM FROM RIPE OLIVES.\*

For the fourth time within a few months a highly fatal outbreak of botulism due to ripe olives is recorded in our columns. The article on an outbreak of botulism in New York in the JOURNAL<sup>1</sup> this week follows close on the heels of the report of the Memphis outbreak in our "General News" of last week. These added to the outbreaks at Canton, Ohio, and Detroit, make a formidable showing.

Three of the four outbreaks appear to have been traced to one brand of olives, packed in southern California, a fact that we believe should be given wide publicity at this time, even if commercial interests suffer. It seems at all events as if all local health authorities should make systematic attempts to find out whether this particular brand of olives is being distributed within their jurisdiction. It is only the part of prudence and good common sense to make sure so far as possible that olives of this brand are not being "salvaged" and perhaps distributed to scores of small groceries and delicatessen shops throughout the country.

Two particularly disturbing features characterize these later outbreaks, one being that the olives apparently responsible for the New York outbreak were not of the same brand as those causing botulism in Canton, Detroit and Memphis. If it is true that more than one brand of olives is involved in the causation of botulism, the difficulties that public health authorities will have in coping with this menace are measurably increased. It is evident also that the whole ripe olive industry should be subjected to investigation and supervision. Steps in this direction have already been taken, as is also noted in our news columns. Thus far green olives do not seem to have been implicated in the causation of botulism.

The second point about which concern may well be felt is the seeming willingness of unscrupulous dealers to sell olives and perhaps other foodstuffs that have been condemned. We are informed that the olives causing death in Memphis were obtained from a store of which the principal business is buying and selling salvaged merchandise. In this case, olives found in a dish on the table at the house where they were served had a very objectionable and pronounced foul odor. In the New York outbreak, a distributing com-

\* From *Jour. Amer. Med. Assoc.*, Feb. 21, 1920.

<sup>1</sup> Sisco, D. L.: "An Outbreak of Botulism," *J. A. M. A.*, Feb. 21, 1920.

pany in New York City refused to put the olives on the market under their label, but the jars were resold by the California olive company that packed them and were shifted about from place to place for some months, many being rejected during their circulation because they were obviously spoiled and unfit for sale. From the information available it does not seem clear that the olives that were eaten in New York had a definitely spoiled odor. The only evidence from those eating the olives came from one victim shortly before death, who stated that he noticed nothing wrong about the odor or taste, and from one 9-year-old child, who also noticed nothing disagreeable in taste or odor. Although a half bottle of ripe olives, probably the one that contained the toxin, was found in the home of the victims, no statement is made about the physical condition of these olives.

It seems clear that immediate and drastic warning should be given to dealers regarding the sale of ripe olives showing any signs of spoiling. It is also true that at least until fuller information is available, salvaged food, particularly olives, should be regarded with considerable suspicion by the general public.

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## ANNOUNCEMENTS.

### A GRANT FOR PHARMACEUTICAL RESEARCH.

The American Pharmaceutical Association has available a sum amounting to about \$450, which will be expended after October 1, 1920, for the encouragement of research. This amount either in full or fractions will be awarded in such manner as will in the judgment of the A. Ph. A. Research Committee produce the greatest good to American pharmaceutical research.

Investigators desiring financial aid in their work will communicate before May first with H. V. Arny, chairman A. Ph. A. Research Committee, 115 West 68th St., New York, giving their past record and outlining the particular line of work for which the grant is desired.

The committee will give each application its careful attention and will make recommendations to the American Pharmaceutical Association at its meeting in Washington, May 3-8, 1920, when the award or awards will be made.

### THE SCIENTIFIC SECTION OF THE A. PH. A.

During the Annual Convention of the American Pharmaceutical Association, which will be held in Washington, D. C., on May 4th to 10th, 1920, the Scientific Section will hold its meetings on Thursday, Friday and Saturday, May 6th, 7th and 8th. Those desiring to read papers before this section should submit them to the Secretary, Dr. A. G. Du Mez, Hygienic Laboratory, U. S. Public Health Service, Washington, D. C., not later than April 1st.

### THE SECTION ON PRACTICAL PHARMACY AND DISPENSING OF THE A. PH. A.

The Section on Practical Pharmacy and Dispensing is endeavoring to make its program for the May Convention Meeting at Washington, unusually attractive and valuable.

Contributors to the Section must get their papers in earlier in the year than usual. In order to get titles and a brief abstract of the papers submitted to the general secretary in time for publication in the main program, it will be quite necessary to have these facts at our disposal early in April.

Practical papers for presentation at our sessions will be welcomed.

Send papers to Ivor Griffith, Secretary, Stetson Hospital, Philadelphia, Pa.

### GOVERNMENT NEEDS CHEMISTS, PHYSICISTS, ETC.

The United States Civil Service Commission announces that the Government service is in need of a large number of chemists of various kinds. During this period of readjustment, technical men are especially needed. Besides chemists it is stated that there are openings for physicists, ceramic assistants, laboratory assistants and aids; metallurgical, technical and electrical laboratorians, etc.

Further information and application blanks may be obtained from the secretary of the U. S. civil service board at Boston, New York, Philadelphia, Atlanta, Cincinnati, Chicago, St. Paul, St. Louis, New Orleans, Seattle, or San Francisco, or from the U. S. Civil Service Commission, Washington, D. C.

### ANNUAL MEETING OF THE AMERICAN DRUG MANUFACTURERS' ASSOCIATION.

The Ninth Annual Meeting of the American Drug Manufacturers' Association will be held at the Hotel Biltmore, New York

City, April 12-15. The Scientific Section will hold a morning and afternoon session on Monday, April 12, and a morning session Tuesday, April 13, while the Biological Section will hold one session only on the afternoon of April 12. The sessions of the Association as a whole will begin on the afternoon of Tuesday, April 13.

The business sessions will be devoid of all purely formal features and will be devoted to practical discussion of important trade problems, notably the alcohol regulations, the return of unsalable goods, freight and express allowances, guarantees against declines in price, and kindred problems.

In connection with the discussion of the alcohol problem, the committee on arrangements hopes to induce Mr. Adams, of the Bureau of Internal Revenue, to address the Convention.

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## NEWS ITEMS AND PERSONAL NOTES.

PHILADELPHIA RECEPTION TO RETURNED SOLDIER AND SAILOR PHARMACISTS.—The various pharmaceutical and drug trade organizations of Philadelphia arranged, through a committee representing these organizations, a public reception and dance for returned soldier and sailor pharmacists. The function was held at Lulu Temple on the evening of Friday, February 27th, and was a marked success.

Mr. Edward T. Hahn was chairman of the committee that made every one of the 800 participants and especially the more than 200 service men feel thoroughly at their ease and enjoy the occasion to the fullest. Among the men who had been in the military service of the country and who made addresses were Karl P. Ehman, who took as a subject, "With the Guns," and Thomas J. Devine, who spoke for "The Navy." A stirring patriotic address by Captain Donald Kirk was followed by a silent tribute in honor of the men who had made the "sublime sacrifice."

Dr. Robert P. Fischelis, chairman of the World War Veteran Section of the American Pharmaceutical Association, presented to each of the service men in attendance a free membership in the A. Ph. A.

Ample refreshments and music interspersed the addresses and the evening was closed with dancing; the occasion was declared as one of the most enjoyable affairs ever held by the drug trade of the Quaker City.

PROF. GREENISH HONORED.—The University of Paris has conferred upon Professor H. G. Greenish, one of the leading pharmacognosts of the world and professor of pharmaceutics to the Pharmaceutical Society of Great Britain, the degree of Doctor, *honoris causa* of the University. American pharmacists are not unacquainted with the work and scientific attainments of Henry George Greenish and, in 1913, in recognition thereof he was elected to Honorary Membership in the American Pharmaceutical Association. He was the recipient of the Hanbury gold medal awarded last year. On the occasion of this additional honor bestowed upon this eminent pharmaceutical authority, the AMERICAN JOURNAL OF PHARMACY is indeed pleased to extend its sincere congratulations.

REMINGTON HONOR MEDAL TO BE AWARDED TO PROF. LLOYD.—The committee of former presidents of the American Pharmaceutical Association upon whom devolves the duty of selecting the recipient for the award of the Joseph P. Remington Memorial Medal, in recognition of exceptional services in behalf of pharmacy, have decided that the medal shall be awarded, in 1920, to Prof. John Uri Lloyd, of Cincinnati, Ohio. The numerous contributions to pharmacy that for many years have come from Prof. Lloyd, his scientific and literary attainments and his devotion to pharmaceutical interests are to be thus commended and honored. The medal has been provided by the New York branch of the A. Ph. A. and the award will be made at an early date at an appropriate opportunity.

THE WOOD ALCOHOL MENACE.—Dean Charles H. LaWall has contributed in *The Forecast* for February a very instructive and popular article on the important subject of "Wood Alcohol—A National Peril." The widest dissemination of the knowledge of the toxic action of wood alcohol and the danger to life and health from its use as an adulterant in beverages, foods and medicines is at this time especially necessary and in this published article we have a happy combination of the scientific and press efforts to make every intelligent person acquainted with this fact. The possibility of toxic action developing even from inhalation of the vapors of methyl alcohol, wood alcohol, when used as a solvent in paints, varnishes, etc., is very rightly presented in the article and the public should be warned against the lurking danger from this otherwise legitimate use of methyl alcohol.

PROFESSOR YOUNGKEN, CONTRIBUTING EDITOR TO BOTANICAL ABSTRACTS.—Prof. Heber W. Youngken, head of the Department of Botany and Pharmacognosy of the Philadelphia College of Pharmacy, has recently accepted the invitation to assume charge of the Section on Pharmaceutical Botany and Pharmacognosy of the important compilation being published as *Botanical Abstracts*.

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## BOOK REVIEWS.

The Eleventh Edition of the THE AMERICAN POCKET MEDICAL DICTIONARY containing the pronunciation and definition of all the principal terms used in Medicine, Surgery, Dentistry, Veterinary Medicine, Nursing and kindred sciences; with over sixty extensive tables; edited by W. A. Newman Dorland, A.M., M.D., has just appeared.

This volume, though handy in size, contains 717 pages. The alphabetical arrangement of words is in heavy type, with definitions in lighter type, facilitating usage. The vocabulary, arranged alphabetically and comprising 682 pages, contains practically all of the modern medical terms. The definitions, although necessarily brief, are quite lucid.

Many tables have been added under their respective headings which correlates much information at a moment's glance. A table of doses in both the Apothecaries' and Metric Systems, embracing 34 pages, concludes the volume.

The spelling of the Alkaloids seems to lack the final "e" as Strychnin, Morphin, Cocain, Codein, etc., while the United States Pharmacopoeia gives the spelling for these Alkaloids with the final "e."

The book, aside from this, takes its place as a good Pocket Medical Dictionary, especially for the medical student.

MITCHELL BERNSTEIN, M.D.

PROCEEDINGS EIGHTH ANNUAL MEETING OF THE AMERICAN DRUG MANUFACTURERS' ASSOCIATION.—The proceedings of the eighth annual meeting of the American Drug Manufacturers' Association, held at the Waldorf Astoria Hotel, New York, March 24-27, 1919, in book form has now been distributed. The initial statement of the "Foreword" that "Between the covers of the book you now

hold is something of direct and practical interest to you, regardless of your position," is fully justified by perusal of this volume. It is certainly different from the stereotyped style of association proceedings of former days. It indicates that the Drug Manufacturers' Association is a live organization and that at its meetings the members are discussing questions of vital importance to the progress of the nation as well as those that are specifically connected with the commerce and manufacture of medicines.

The address of the President and the report of the Secretary present much food for thought in the various topics presented under such headings as "Tendencies Toward Socialism," "The High Cost of Paternal Legislation," "Politics and the High Cost of Living," and "Evils of Blind Partisanship."

The discussions upon legislation, both enacted and proposed, are enlightening and it would be well indeed if many of those interested in the various branches of the drug trade would read and study these. The various questions of especial interest as trade problems are not at all sidetracked nor were the scientific matters overlooked. The Proceedings of the Scientific Section, formerly the Committee on Standards and Deterioration, present a number of valuable scientific and research questions that had been under consideration during the year and the findings will prove of material aid in the revision of official standards already established and in fixing proper tests for some other substances for which standards have not been definitely determined.

G. M. B.

DIGEST OF COMMENTS ON THE PHARMACOPOEIA OF THE UNITED STATES OF AMERICA AND ON THE NATIONAL FORMULARY FOR THE CALENDAR YEARS 1915 AND 1916.—These two pamphlet publications comprising *Hygienic Laboratory Bulletins*, 118 and 119, have been compiled by A. G. Du Mez of the Division of Pharmacology and carry on for two more years the work of compiling the criticisms upon our legal authorities for standards for drugs. The books now in hand continue the same general style of presenting the subjects as adopted with the inception of this work by the late M. I. Wilbert. The United States Public Health Service in undertaking this important piece of work and continuing same systematically is performing a notable service to all of the interests concerned in the establishment of correct standards for medicines and indirectly is performing a valuable service to the public who are the final consumers and whom it is aimed to serve.

G. M. B.

## OBITUARY.

## EUGÈNE COLLIN.

In the decease of Eugène-Jean-Baptiste Collin on December 22, 1919, France has lost one of her most prominent scientists who occupied a prëminent position in the field of microscopy and anatomical structure of drugs and foods and who had devoted his life in a modest yet most effective manner to scientific study. He was born at Carignan, Ardennes, on June 22, 1845. At an early age he obtained his education as bachelor of letters and sciences and then applied himself to pharmacy. He was a hospital interne in 1868 and during this period wrote his first paper on *materia medica* for which he was awarded the first prize.

In 1871 he arrived at the distinction of a pharmacist, first-class, and on this occasion presented a thesis on the structure of the official rhubarbs. He determined to apply himself to the microscopic study of drugs and foods and the detection of adulterants and sophistications, a branch of science which at that time was but little explored. His investigations covered a multitude of substances and his contributions to scientific literature were numerous and on a diversity of subjects. Among these may be mentioned his studies of starches, canella, pepper, coffee, tea, cinchona, cantharides and marjoram.

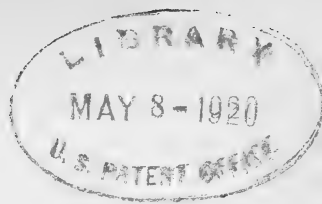
Associated with another name familiar to students of botany of drug plants there was published "The Vegetable Origin of Simple Drugs," by Planchon and Collin, in which Collin prepared the major portion of the work. In 1894, he published "A Guide to the Practical Determination of Officinal Powders;" in 1902 appeared his "Précis de *Materia Médicale*;" and in 1907 a "Treatise on Vegetable Toxicology," being a study of the application of the microscope to the study of the vegetable poisons. In 1905, there was published "An Anatomical Atlas of Vegetable Drugs," by Henry George Greenish and Eugène Collin.

His work was not without due appreciation and recognition and Collin was elected to honorary membership in many pharmaceutical societies. He was an honorary member of the Philadelphia College of Pharmacy and only last year was elected to honorary membership in the American Pharmaceutical Association. He received the award of the Hanbury medal in 1903.

By appointment of the Minister of Commerce, he held the position of microscopist in the central laboratory for the suppression of frauds and here his work for many years, and especially during the world war, is said to have been of inestimable value to his fellow countrymen.

G. M. B.





# THE AMERICAN JOURNAL OF PHARMACY

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APRIL, 1920

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## EDITORIAL.

### THE INSUFFICIENCY OF PHARMACEUTICAL EDUCATION.

Nearly one hundred years have elapsed since the first school of pharmacy was established in America. In this initial systematic effort to educate pharmacists a course of two years, consisting of lectures on materia medica and chemistry, was the original conception of the special education necessary for the would-be druggist. A practical experience of four years in a drug store was then, as now, considered by those engaged in the calling as essential to complete the equipment and training necessary for an apothecary. During this time, the student by faithful application to his studies and store duties was presumed to have acquired the requisite scientific knowledge and professional skill and to have become proficient in the art and practice of pharmacy.

In those early days, little or no attention was paid to the preliminary education of the would-be pharmacist. Yet as one studies the history of those who were active in pharmacy during this period, he is convinced that many of these were men of high attainments and great ability and exceptionally well educated for the time in the sciences and languages. The thoughtfulness of parents in selecting vocations for their sons coupled with the scientific and professional associations of the apothecary, it would seem had attracted many of the young men with scientific propensities.

For many years the colleges of pharmacy did not deem it necessary to require of their matriculants any standard or grade of preliminary education. Reliance upon the final examinations to weed out the undesirables and incompetents seems to have been the only method considered expedient. With the changes of time, the ideals have been elevated and from time to time the preliminary education re-

quired of those entering schools of pharmacy has been advanced and in the near future all students admitted to the recognized schools of pharmacy in the United States will have had at least a preliminary education, the equivalent of a standard four years' high school course.

The American Conference of Pharmaceutical Faculties has been a potent factor in determining that prerequisite education was an initial step that must be taken to establish pharmacy on a professional basis. A number of the states now require by enactment that those licensed to practice pharmacy must be graduates from approved schools of pharmacy and prior to such pharmaceutical education shall have had a standard fundamental education. It is imperative that such laws should be enacted in every state so that prerequisite education for pharmacists will be a universal requirement in the United States.

The claim that this would work a hardship cannot be maintained as throughout the United States opportunity is now afforded, through the public school system, for every youth to acquire at least a high school education. When the first school of pharmacy was established, and for some years thereafter, it was the exceptional boy or girl who had the opportunity of attending high school, but now this is the common privilege of all.

While pharmaceutic educators have been making strenuous efforts to provide for a fundamental education, they have not paid the attention deserved to the necessity for a more thorough training of their graduates. With the great advances made in the medical profession and the constant additions to our *materia medica* and the progress of the sciences, the knowledge required of the pharmacist is necessarily many times that expected a century ago. The colleges have endeavored to supply this extended knowledge by establishing chairs and instructions in many branches of science that were never dreamed of as essential to pharmacy in the earlier decades of pharmaceutical education in America. Pharmacognosy, bacteriology, clinical and pathological chemistry and pharmacodynamic assaying and commercial training are only some of the courses that have been introduced into the collegiate education and many of these are included in the courses outlined in the Pharmaceutical Syllabus.

Despite the fact that these added courses mean many hours of additional study and application and likewise that the commercial aspect of pharmacy must receive increased attention from the students, the colleges are still attempting to impart the fundamental

knowledge required of the pharmacist in a course of two years. Under the conditions existing it is apparent that this becomes an effort in which both the teachers and the students are endeavoring to accomplish in a period of two years, what, if accomplished in a period of four years, would be very creditable and more satisfactory.

The attempt to give in a two-year course an ample foundation for the practice of pharmacy is a serious defect in our present system of pharmaceutical education. The average student gets a confused and unsatisfactory education in the time allotted and it is not to be wondered at that his future career is devoted more to the commercial than to the professional aspect of his calling.

The first duty of the educators is to make good, practical, well-equipped pharmacists. Ideals of pharmacy must be based upon a thorough foundation and if pharmacy is to be developed into the professional status we are hoping and working for, it will be necessary that the majority of those engaged in the calling shall have a thorough education and be fittingly prepared for professional careers.

The student who takes up post-graduate studies and fits himself to carry on the higher professional duties of analyst or expert in pharmacognosy or bacteriology is the exception, and this limited number cannot establish a professional status for the entire body engaged in the calling of pharmacy.

The time that should be required by the average student to perfect himself in the theoretical education of a pharmacist and likewise in the commercial training must be greatly extended if we expect to have a sufficient amount of knowledge absorbed by the entire body pharmaceutic to claim professional status.

The need for extending the time required for obtaining a professional education has been recognized by medicine, law and theology and in fact by practically every other profession than pharmacy. For some reason the pharmacy schools have continued in their attempt to educate professional pharmacists in a course of two years. The necessity for greatly extending the time devoted for the education of students in pharmacy is so apparent that the directing of the attention of educators thereto should be unnecessary.

To obtain the professional rank we desire to secure for pharmacy, the future graduate must be better equipped, and this can only be accomplished by extending the time devoted to the ever-increasing studies. The time is certainly at hand when the *fundamental course*

for the training of pharmacists should be extended to at least three years of collegiate education.

G. M. B.

## CALCREOSE PROTECTED BY UNITED STATES PATENT.

In the January number we republished from *The Prescriber* of December, 1919, an article on calcium-creosote. In this reference was made to Calcreose, and a formula for the preparation of a similar compound in liquid form given in the *Pharmaceutical Journal*, was republished.

We are in receipt of a communication from the Maltbie Chemical Company, of Newark, New Jersey, in which we are advised that the process for making Calcreose is patented, and that no one can make an imitation without infringing upon their patent.

We republished this paper as a contribution to the knowledge of the use of creosote as a remedial agent and the fact that Calcreose was protected by process patents entirely escaped our consideration.

It is not the purpose of the AMERICAN JOURNAL OF PHARMACY to submit to our readers the possibilities of imitating a patent-protected commercial article, nor have we intended in any way at any time to condone substitution or any other unfair practice in dispensing. On the contrary, the JOURNAL has always maintained the position that it was plainly the duty of the pharmacist to dispense the original proprietary or patented articles in all cases where such are prescribed, and the manufacturers of Calcreose have our assurance that it was not our purpose to suggest any substitution for Calcreose.

We have not read the patent specifications in which the claim for novelty of invention or discovery is set forth, and we are not prepared to express our opinion as to the similarity of the liquid preparation yielded by the formula from the *Pharmaceutical Journal* to the powdered product described in the article as Calcreose.

That creosote is a mixture of phenols and phenol derivatives obtained by the distillation of wood tar is asserted by the United States Pharmacopoeia. The phenolic character of guaiacol and creosol, the chief constituents of official creosote, is well established, and it has long been a matter of common knowledge that phenols as a class unite with basic elements such as potassium, sodium and calcium, and that the presence of water facilitates the formation of such compounds. Under these circumstances, the defense of such

a patent as a novel or original invention might become an interesting problem. G. M. B.

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## AMERICAN PHARMACEUTICAL ASSOCIATION MEETING.

BY L. F. KEBLER, CHAIRMAN PUBLICITY,

WASHINGTON, D. C., MAY 5 TO 10, 1920.

Everybody wants to see Washington. During the recent Titanic War the eyes of the entire world were turned to the United States and since its termination Washington easily holds first place in the universe. The mecca of the world is Washington. It is the hope and ambition of every good citizen of our great country to see his National Capital at least once. There is more here than can be seen and learned in weeks of sightseeing and study. We have things in Washington that will fascinate any one from the most profound scientist or astute statesman, to the merry sightseers. Our beautiful city and the internal workings of the greatest government on earth fascinate and properly so, all comers. Hotel accommodations are among the best.

Of all the months May is the most charming. It is then that the new, fresh foliage of numerous and rare trees will overhang our broad and well-paved streets. The many parks and parklets, with native and exotic plants, will be in their best attire. The animals in our charming, rolling Zoölogical Park will bring joy and pleasure to all lovers of nature. It is the time of year when life is bubbling over. Everything will be all activity. The rugged, scenic, Great Falls of the Potomac are but 20 miles away. The ladies have planned a trip to this beautiful spot.

In Washington can be seen the numerous and beautiful, massive Government buildings of Doric, Ionic and Gothic architecture. Next May will be the best time to see and learn how the government business is carried on. Congress will be in session. You should spend several days at the Capitol and see how the Senate and House conduct the nation's business. Trips should be taken to the White House, the Congressional Library, Pan-American Building, D. A. R.

Hall, Washington Monument, Lincoln's Memorial, National Museum, Smithsonian Institution, Zoölogical Garden, Botanical Gardens, Bureau of Printing and Engraving, Corcoran Art Gallery, Fish Commission, Government Printing Office, Lee's Mansion, etc. Provisions are made to take all the visitors to Mt. Vernon enroute to the Shad Bake.

The local committee is prepared to give every possible assistance and aid in planning so that you can see and learn the greatest amount in the shortest possible time. There will be some one at the Union Station, properly badged, to meet you. If you should be missed apply at the Traveler's Aid Booth, in the center of the building, for information. There is only one railroad station in Washington and that is considered the best in the world, by many. Its main concourse will accommodate 50,000 people. On arriving in Washington go directly to headquarters, The New Willard Hotel, for registration and information. Cars passing in front of the station marked "Georgetown" or "14th" and some other street will take you to headquarters.

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#### 1820—A BIT OF HISTORY.\*

BY J. W. STURMER, PHAR.D.

There is no periodicity in the great events which mark the march of human progress. Only happenings correlated to the seasons keep step with the calendar. And when history repeats itself—which it never does except with variations—even numbers of years, or odd numbers, or decimal multiples, have no special significance—of course not.

But it is true that the year 1820 was in many respects like the present—1920. The chronicles of that early period seem strangely modern. We find references to high prices, labor disturbances, to unstable equilibrium in business affairs, political unrest, and evidence, in Europe particularly, of that abnormal attitude of mind which in our time has led to overt acts on a large scale, and which has received a Russian name. The fact is, after a hundred years Europe and America, both, again are passing through a period of convalescence following the exhausting distemper, war. In 1820,

\* Extracts from an address before Philadelphia Branch, A. Ph. A., at the January meeting.

as at present, Europe was battle-scarred, then as a result of the campaigns of Napoleon. America was battle-scarred, too, for the burning of Washington and the victory of New Orleans were still discussed as recent happenings. Men had gone to war; some had not returned. Many industries had been ruined. Certainly America in 1920 can realize the conditions which obtained a hundred years ago. In 1914 America could not have done so.

But despite conditions seemingly so unfavorable, the period of 1820 marks a glorious renaissance in science and art. In literature, during the war period, or immediately thereafter, Moore, Shelley, Wordsworth, Keats, Byron, DeQuincy, Scott, Coleridge, Lamb, Goethe, Victor Hugo, were producing masterpieces; yes, and Washington Irving and J. Fenimore Cooper. It was the era of the romantic movement, the greatest manifestation of literary genius since the time of Shakespeare.

Of composers there were Beethoven, and Schubert, and Mendelssohn, and other masters of the first rank. It was a golden age in music.

In science, there were Berzelius, Humphrey Davy, Faraday, Cuvier, Dalton, Drummond, Gay Lussac, Proust. It was the dawn of the modern productive era of science, which has continued to the present time, making the last hundred years the most prolific in discovery in the history of the human race.

True enough, every sequence is not necessarily a consequence. And wars in the past have not without exception been followed by a notable advance in the conquest of nature. But who will question that the great war exploits which terminated with Waterloo and New Orleans did not stir to the depths the emotions of men, inspiring writers, composers, painters, and also men of science, and in the latter awakening imaginative faculties, so useful in research? And if this be true, may we not expect that the stupendous struggle so recently ended will also be followed by a pronounced quickening of creative and inventive genius? And, if so, we may be sure, America will furnish its generous share in results.

In 1820, America could not be expected to figure prominently in art or science. Our country was new. The population was a largely rural. A considerable proportion was distributed over vast areas but sparsely settled, where life was rather primitive, and where men were hard put to it to provide the elemental needs—food, clothing, shelter—then medical service for the sick, rudimentary schooling for the children. And when the scientists of the old world

were engaged in extending the frontier of human knowledge, many of our most resourceful Americans were engaged in pushing the frontier of the white man's civilization westward. In 1820 the great migration over the Indian trails, which had been transformed into roads, was in full swing. On the Conestoga Road, the covered wagons of the travelers, headed for the land of mystery, adventure, opportunity—the West—were as numerous as the stannic "Lizzies" on our mountain roads during the summer months of more recent years. These men, who with their families, their lares and penates, were moving toward the setting sun, were principally farmers. But with them traveled the carpenter, the mason, the blacksmith, the miller and the millwright, the merchant, the doctor, and the apothecary. When a town of some size had developed, in due course, there appeared the apothecary shop, and the ring of the pestle proclaimed that medicines were being prepared *secundem artem*. And who will say that the inventive genius displayed by our pioneer doctors and apothecaries, in adapting limited resources to many and diverse needs, was not—in certain instances at least—as great as that of many a European research worker who by virtue of his better facilities succeeded in getting results which warranted their being recorded in the annals of science?

This was a truly heroic period in our country's history; it was the period of nation building, the various phases of which absorbed a large share of the energies of energetic men—the men with initiative. "In the four quarters of the globe, who reads an American book? Or goes to an American play? Or looks at an American picture? What does the world yet owe to American physicians and surgeons? What new substances have their chemists discovered, or what old ones have they analyzed?" Thus wrote Sydney Smith in the January number of the *Edinburg Review* in the year 1820. We need not take issue with him, although he was seemingly quite ignorant of American progress. Indeed, we may admit frankly that books of the first rank were not yet numerous. Odysseus was too busy to devote time to the composing of Odysseys. But some promising youngsters were playing marbles in American school yards—Whittier, Longfellow, Emerson, Hawthorne, Holmes—to mention a few; and in this year of the Missouri Compromise, 1820, the author of the Gettysburg address was doing his chores on a primitive Indiana farm.

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American science and American art were in the formative period. There were houses to erect, bridges to build, canals to dig, roads to be made passable. Just as American literature was principally political in character, American science was largely applied science, and art, industrial. As for the pharmacist, he was busy in providing the most necessary medicaments, and had, speaking generally, as yet no leisure for scientific experimentation.

We must not overlook the fact, however, that at a time when America as a whole was still in the pioneer stage, the older and more densely populated districts near the Atlantic seaboard, had attained to a high degree of culture. Here we find the colleges and universities of that period, and the learned societies, and the literary organizations, and the book publishers. It is here that we must look for the first developments in pharmacy.

In 1820, Philadelphia, which had served as the national capital, and where all the great Americans of the early days had sojourned, the largest city in the country at that time, with 130,000 inhabitants, an important seaport, in close touch with the old world civilization—Philadelphia, the seat of a university, and of the Institute founded by Franklin—became, as a matter of course, a center of learning. And medical sciences found here a particularly favorable atmosphere for growth. And hand in hand with the progress in medicine, we find the early progress of pharmacy.

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To be sure the apothecary of 1820 was practicing his art as it had been developed in Europe. If he was American-born, he had, in all probability, received his training under an apothecary who in turn had been an apprentice in a European pharmacy. If he was a rather recent accession to the population, he used, as a matter of course, the methods and the textbooks of his native land. The pharmacopoeias of London, Edinburg and Dublin were at that time in constant use. Uniformity of practice was conspicuous by its absence; for there was no pharmacopoeia as yet for this new nation; nor were there any purity standards for drugs or medicines. As for legislative regulations governing the practice of pharmacy, no laws of that character had as yet been passed. There were neither pharmaceutical organizations nor pharmaceutical journals. The important textbooks for pharmacists, with the exception of the American Dispensatory, then already in its fourth edition, were foreign.

The drugs which the apothecary had on his shelves were imported; and so were also his bottles, his jars, and in fact, even his window-panes, which made up his odd little show-windows. At this time, when Fulton's great invention, the steamboat, was still a novelty, and the word sailor still had its original meaning, the Delaware harbored ships from the most distant shores. And the inventories of cargoes, as published in the old time newspapers, include a large and varied list of drugs. It is from these inventories, in fact, that one may best reconstruct the old-time drug stock, for very few indigenous medicinal plants had received recognition. Here are some of the drugs which were deemed important in 1820—for they were obtained from overseas in large quantities: Aconite, Aloes, Asafetida, Belladonna, Benzoin, Camphor, Cantharidis, Capsicum, Castile Soap, Cinchona, Colchicum, Colocynth, Copaiba, Cubeb, Ipecac, Gamboge, Licorice Root, Licorice Extract, Hyoscyamus, Jalap, Lobelia, Myrrh, Nux Vomica, Opium, Rhubarb, Castor Oil, Sarsaparilla, Scammony, Squill, Tolu, Tragacanth, Valerian, Veratrum Album, Veratrum Viridi, Ginger. Yes, the general aspect of the 1820 drug store, with its old-fashioned shelf-ware, was odd enough; but the antique bottles held drugs which have retained their popularity to the present day.

The apothecary's stock was, however, not limited to vegetable drugs; he had a sundry supply of chemicals, as follows: Hydrochloric Acid, Nitric Acid, Sulphuric Acid, Citric Acid, Arsenic, Alum, Ammonium Chloride, Black Antimony, Barium Sulphate, Lime, Chalk, Marble, Copper Subacetate, Copper Sulphate, Prussian Blue, Sulphate of Iron, Mercury, Calomel, Corrosive Sublimate, Magnesium Carbonate, Magnesium Sulphate, Lead Oxide, White, Lead, Saltpeter, Potassium Carbonate, Cream of Tartar, Salt, Borax, Sodium Carbonate, Sodium Sulphate, Zinc Carbonate and Zinc Sulphate. His stock included the elements, Antimony, Bismuth, Copper, Iron, Mercury, Lead, Zinc, and Sulphur. These chemicals he bought, for they were even then made industrially.

But many chemicals now made exclusively on the industrial scale were early in the nineteenth century made by the apothecary in his own little laboratory. To be sure, there were some then, as at present, who chose to buy rather than to manufacture. But the list of chemicals actually made in stores at that time is surprisingly large, and included the following: Solution of Ammonium Acetate, Tartar Emetic, Solution of Magnesium Bicarbonate, Silver Nitrate,

Solution of Potassium Arsenite, Subnitrate of Bismuth, Lead Plaster, Iron Acetate, Iron Carbonate, Iron Oxide, Red Oxide of Mercury, Subsulphate of Mercury, Potassium Acetate, Rochelle Salt, Sodium Phosphate, Ointment of Mercuric Nitrate, Zinc Acetate and Zinc Oxide.

Of pharmaceutical preparations there was a large and varied list. It included Medicated Waters, Medicated Wines, Medicated Honeys, Medicated Vinegars, Spirits, Infusions, Decoctions (made when required), Tinctures (made by maceration—10 days) Solid Extracts, Mixtures, (some of which were Emulsions), Liniments, Ointments, Cerates, Plasters, Pills, Powders, and Confections.

It is indeed strange that the furniture and shelf-ware and equipment of the apothecary should have become in a hundred years so strikingly antique, while the materials which he dispensed, and with which he worked, should to so large a degree have continued in use uninterruptedly to the present day. How many drugs in the old inventories of ship cargoes are now obsolete? Very few. And as to preparations note how many have passed through nine pharmacopoeial revisions, experiencing radical alterations, but not deletions.

Nor should we picture the apothecary himself as an aged recluse, sitting at his desk, dressed in medieval garb, with metal-rimmed spectacles on his nose, "dandruff on his coat collar and a far-away look in his eye," sitting there inactive, surrounded by alembics and other gimcracks of the alchemist's stage properties—a man with whom we have nothing in common. For then, as at present, men were old, or young, or middle-aged; and they exhibited many variations in personality. But we may be quite sure that the apothecaries of 1820, living at a period of great activity, when stirring events were transpiring, when political interest was keen, when Philadelphia was conspicuously progressive, when the men of the hour were men of action—that these old-time pill rollers lived an active and full life, with varied interests—and were factors in this community.

But they indited no books. They published but little. The histories of Old Philadelphia fail to chronicle their doings. Their shops and stocks have disappeared. The very buildings in which they lived and worked have, in many cases, made room for larger structures of modern architecture. Yes, the old apothecaries of Philadelphia have vanished. "Like streaks of morning clouds they have melted into the infinite azure of the past."

The beginning of a new year always induces a retrospective mood,

and it may even lead us to read history. But why should we have a particular interest in 1820, aside from the interest which attaches to a time an even hundred years ago? The fact is, 1820 marks the close of an epoch. It marks the time when pharmacy, until then wholly dominated by European thought and precedent, awakened to its opportunity and struck for a certain independence. That very year the first national pharmacopoeia was issued. A few months later, in Carpenter's Hall, the first organization of apothecaries was formed. And a few months after that, this organization—The Philadelphia College of Apothecaries—opened its doors for the first session and for the first class of American students in pharmacy.

Hence, 1820 has a special significance for pharmacy.

What 1776 is to us as Americans, 1820 is to us as American pharmacists.

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## COMMENTS ON MAGENDIE'S FORMULARY.\*

BY CHARLES H. LAWALL, PH.M.

PHILADELPHIA, PA.

Books reflect the spirit of the time in which they were written as well as the knowledge of their authors.

Few books in science outlast more than a decade, or so, of active utility; after that they are usually of value only for occasional reference, and a scientific book which is nearly a century old is more interesting as a curiosity than for any practical value it may have in the science to which it relates.

It is interesting, however, to carefully review one of these older books occasionally to bring one to a realizing sense of how conditions have changed during a given period of time.

In pharmacy, medicine and chemistry such surveys are of peculiar value, for not only has there been a revolutionary change in the practice of each of these professions but the very nomenclature has undergone such a metamorphosis that the student of to-day would often find much of the text unintelligible without the use of a glossary.

Magendie's Formulary is a small book issued in an English translation in 1824. The book is of peculiar interest to pharmacists, chem-

\* Read at the meeting of the Philadelphia Branch of the American Pharmaceutical Association.

ists and physicians as will soon be seen by a discussion of some of the details of its subject matter. Its translator, Robley Dunglison, M.D., was widely known as a medical author in the early part of the last century and published a medical dictionary which attained great popularity and went through many editions.

The title page itself is noteworthy for it is called a "Formulary for the Preparation and Mode of Employing Several New Remedies: namely, Morphine, Iodine, Quinine, Cinchonine, The Hydrocyanic Acid, Narcotine, Strychnine, Nux Vomica, Emetine, Atropine, Picrotoxine, Brucine, Lupuline, etc., etc."

To place oneself in the mental attitude of a period in which Morphine, Iodine, Quinine, etc., are heralded as new remedies requires some intellectual exertion, but fortunately the translator in his preface makes this easier by the quaintness of his language and the ingenuousness and frankness of his views and expressions.

He states: "Great credit is due to the French chemists, and especially to M. M. Pelletier and Caventou, for having discovered that the active principle of several of our chief remedies resides in peculiar alkalis; and also for isolating these alkalis so that they may be used in practice according to a determinate and intelligent principle. Great praise is also due to M. Magendie for the indefatigable way in which he has investigated the action of these new alkalis on the human body."

Here already we see evidences of the transferring from pharmacy to chemistry the credit for worthy achievements, for Joseph Bienaime Caventou (1795-1877) and Joseph Pelletier (1788-1842) were prominent pharmacists of their day in their native city of Paris. In 1820 when these two brilliant pharmaceutical workers discovered and named quinine, Pelletier was 32 and Caventou 25 years of age. In those days many important and epoch making discoveries were made by comparatively young men. Wöhler who revolutionized synthetic chemistry a few years later by the transformation of ammonium cyanate into urea, was only 28 years old at the time of this discovery.

Continuing, the translator says: "To druggists and to operative apothecaries it must be acceptable to have thus collected a full account of the mode of preparing these different alkalis."

This would indicate a more specific and distinctive use of these terms than is now accorded them. It is probable that the distinction lay in the fact that druggists were simply dispensers while operative apothecaries manufactured as well as dispensed.

After commenting upon Magendie's observations concerning the use of these "vegetable alkalis," which were not yet called "alkaloids," the translator continues, in partial disagreement, as follows:

"There exists, however, an objection to the principle of thus isolating and concentrating the active part of our remedies. Perhaps every practitioner feels that medicinal substances are more efficacious as they are presented to us combined by the Hand of Nature, than when their active part is isolated and recombined by the hand of man. Thus, then we are all inclined to give our remedies in substance, as it is called, rather than as prepared by the chemist or the druggist, and we are only deterred from using these natural preparations by the greater bulk, and other inconvenient properties of them, as compared with our more artificial preparations. Thus, also, we all feel that our artificial mineral waters, however accurately they may imitate the natural ones, do not produce the same good effect as those natural ones do; and even some of them, for instance, the bath waters, appear on analysis to be so pure and free from extraneous ingredients that we are reduced to the necessity of attributing their often powerful effects to the presence of some evanescent principle, which cannot be detected by chemical analysis."

Is this latter thought a prophecy of the discovery of radio activity? In this paragraph, too, the use of the word chemist as applied by an American translator to one who is concerned with the preparation of medicines, indicates again the close correlation at that time between chemistry and pharmacy. The word pharmacist was not then in general use in America and the word chemist here seems to be used synonymously with the word apothecary of the earlier paragraph.

In another paragraph the translator mirrors the sentiment of the times with respect to new remedies in a way that shows conditions to have been much as they are now, he says, speaking of himself in the third person as was the custom:

"He is almost angry when he sees the popular authors of the day sneering at the introduction of new remedies and saying in ignorant self conceit, 'Ay, here they come, one after another, vaunted to the skies for properties which sober investigation shows not to belong to them; we shall soon see them laid upon the shelf until they are again held up to the world as prodigies by some future enthusiastic searchers after novelty.'"

I wonder whether any other work ever heralded as new remedies

such a constellation of stars of the first magnitude as those given in Magendie's little book.

Many additional interesting views are then given by the translator who develops quite a narrative style at times and concludes as follows:

"The translator has added notes, which comprise a reference, he believes, to almost all the authorities on the subjects treated of. He wishes he could add records of the several remedies having been employed by British practitioners; but, with the exception of the prussic acid and iodine, which have been somewhat extensively used, he believes that the other preparations have not even been seen in this country, except as matters of curiosity. It were to be wished that M. Magendie had given the particulars of his experience of their prescription in the human subject. Several French journals, and especially his own excellent *Journal de Physiologie*, contain an abundance of cases in which the Sulphate of Quinine has been used with marked benefit in the latter stages of malignant fevers, in all forms of intermittent fever, and especially in many varieties of neuralgia; but the translator is ignorant that any published cases exist in which other alkalis have been employed."

In the author's preface, which is quite short by comparison with that of the translator, the following interesting statements occur:

"In spite of the opposition of the physicians of the seventeenth century (notwithstanding the celebrated decree of parliament which prescribed tartar emetic, and in spite of the spiritual sarcasms of Guy Patin), the utility of antimonial remedies has been long recognized. For once, at least, prejudice gave way before evidence. \* \* \*

These substances \* \* \* \* act, when given in small doses. Every principle which might mask or hinder their action has been separated from them; their effects bear a decisive character which cannot be misunderstood for they have been studied with care both on animals and on man when in health and when in disease; a perfect knowledge of their chemical properties and great accuracy in their mode of preparation are sufficient to secure uniformity with regard to their strength and manner of action; and, lastly, each of them forms a medicine in its most simple and energetic state.

"Time alone can pronounce definitively on the advantages and inconveniences of these new remedies; but which ever way it may be, the following pages may be useful, by teaching the mode of preparing them without making it necessary to consult general treatises in

chemistry, or pharmacy; and by giving medical men every facility in submitting them to personal experience, which is frequently, after all, the only truly profitable course.

"I shall feel extremely grateful for any critical or other remarks appertaining to the substances treated of in this work. To those of my medical brethren who may be kind enough to address them to me, I return my thanks beforehand; and I shall hasten to turn them to the improvement of science, by inserting them in the next edition."

The book itself is a small duodecimo volume printed in Philadelphia in 1824. It consists of 268 pages.

The principal portion or about two-thirds of the book concerns itself with the detailed consideration of the "New Remedies" mentioned in the title, an enumeration of which will be interesting, each of the following subjects being accorded a separate section or chapter:

Morphine	Veratrine
Narcotine	Hydrocyanic Acid
Extract of Opium deprived of Narcotine	Solanine
Extract of Opium deprived of Morphine	Atropine
Iodine	Daturine
Resin of the Nux Vomica	Hyoscyamine
Strychnine	Delphinine
Emetine	Picrotoxine
Pure Emetine	Gentianine
Cytisine	Lupuline
Cinchonine and Quinine	Brucine
Esculine	

There is also given in this portion of the book a posological table and a table of preparations and their strengths in active principle.

There are three appendices to the book: Number one, containing a list of preparations and their compounds. Appendix number two concerns itself with poisons of mineral, vegetable and animal nature. Appendix number three is devoted to the "Art of Prescribing," with numerous detailed examples of prescriptions for various kinds of symptoms and diseases. An index completes the book.

Before commenting upon any of the details of the book in a systematic manner it may be well to make some general observations.

One of the first things to attract the attention as one scans the book



is the fact that the subject of weights and measures must have been in a transition state when the book was written, as there are parenthetic notes everywhere of which the following examples may be given:

- 1 lb. (15 oz. 6 dr. 1 grain troy)
- 1 oz. (7 dr. 52.5 grains troy)
- 1 gros (59 grains troy)
- 4 grains (3.28 grains troy)
- 1 grain (0.82 grain troy)

This is very confusing in the light of modern practice and even when taking into consideration the pharmaceutical history of weight systems and their fluctuations. In the first place it indicates two different standards for the grain in actual use, some light is thrown upon this in one portion of the book where it is stated, 1 grain Fr. (grain 0.82 troy). As Magendie was a French physician, the system was likely a French system. Calculating it in terms of troy grains the pound must have weighed 7561 grains troy and the ounce 472.5 grains troy, the gros (59 grains troy) was evidently the eighth part of this ounce.

It is odd, too, that Magendie should not employ the metric system, as it had been in use for some years in France. The only reference to it is found in several formulas where the liquid is directed in litres, while the solids are directed in grains, a jumbling together of the old and the new.

Another interesting impression gained by a general survey of the book is the list of substances and preparations unfamiliar to the pharmaceutical practice of to-day. Notable among these are Testarum Praeparatum (prepared oyster shells), Castoreum Ros-sicum (glands from the Russian beaver), Cuprum Ammoniatum, Ferrum Ammoniatum, Syrupus Mori (syrup of mulberries), Infusum Armoraciae Composition (compound infusion of horse radish). Burnt oyster shell, burnt hartshorn and burnt sponge all seem to have been in use at that time.

The nomenclature, too, must call for passing comment. Sub-carbonate was the term employed then where we now employ bi-carbonate. Antimonium Tartarizatum was the older name for Tartar Emetic. Hydrargyri Submurias for calomel and Hydrargyri Oxymurias for corrosive sublimate, would look strange on a modern prescription. Tinctura Lyttæ was the former name for Tincture of Cantharides. Turnsol paper was an indicator then used as we

now use litmus paper. The words chloruret for chloride and super-tartrate for bitartrate are still intelligible.

One of the odd things noted is that Iceland Moss (*Cetraria*) was called Liverwort, and another that Opium was classed with the gum-resins.

One striking difference from modern books covering similar ground is the complete absence of chemical symbols or formulas. Although Dalton's atomic theory had been published fifteen years prior to the appearance of this work it is apparent that it had not been generally accepted, at least by authors in other countries.

The most outstanding feature of a cursory study of the book is the great amount of credit given to pharmacists for discoveries of value, among the pharmacists thus honored are Derosne, Pelletier, Caven-tou, Serturner, Boullay, Robiquet, Hecht, Henry, Pessina, Desfosses, Vauquelin and Brandes. This reminds us of the fact that the pharmacy of that period embraced not only what is now considered the professional side of pharmacy but much of chemistry as well. Many of those who became prominently identified with the development of chemistry obtained their training and experience in the practice of pharmacy and some, as Vauquelin, remained prominently identified with pharmacy during the whole of their subsequent careers.

Medicine was more dependent upon pharmacy than is the case to-day and there being no large pharmaceutical nor chemical manufacturing establishments; where scientific progress depends largely upon commercial exploitations of the product, there seems to have been a larger number of scientific workers at that time who were interested solely for the sake of the discoveries which could be made, than at any subsequent period of medical and pharmaceutical development.

It is not the intention in this brief review of the book to make critical study of the subject matter. It is intended only to give to one who has not seen the book an idea of its scope and character and to point out details of peculiar or particular interest. Thirty-five pages are given to the consideration of the manufacture of *Morphine* and the preparation of the acetate and sulphate of the alkaloid with comments upon their physiological action. It is stated that the result of the analysis of opium by Derosne, Serturner and Robiquet, shows opium to be composed of the following constituents: (1) Fixed oil; (2) matter analogous to caoutchouc; (3) a vegeto-animal substance not fully investigated; (4) mucilage; (5) feculent matter

(starch); (6) resin; (7) vegetable fibre; (8) narcotine; (9) meconic acid; (10) another unidentified acid discovered by Robiquet (probably lactic); (11) morphine. This list of constituents, excepting for the alkaloids, is in close accord with modern teaching and speaks well for the thoroughness of the work done by these early apothecary-chemists.

The composition of morphine is stated in percentage terms as follows:

	%	%
Carbon.....	72.00	71.7
Nitrogen.....	5.50	4.9
Hydrogen.....	5.50	6.7
Oxygen.....	17.00	16.7

The figures in the second column are present figures.

The comparison with the modern figures, shows a creditable degree of accuracy for the ultimate analysis of the time and for the atomic weights that were used in the calculation.

A Syrup of Acetate of Morphine containing 4 grains to the pound is recommended as well as a Syrup of Sulphate of Morphine of similar strength.

A formula is also given for a preparation called *Guttae Anodynae* (Anodyne Drops) which is as follows:

Acetate of Morphine.....	16 grains (13.12 grains troy)
Distilled Water.....	1 ounce (7 dr. 52.5 grains troy)
Acetic Acid.....	3 or 4 drops
Alcohol.....	1 gros (59 grains troy)

These drops, it is stated, are a good substitute for liquid laudanum, Rosseaus drops, tincture of opium, etc.

We here recognize an old friend which for many years was known, not by the name proposed by its author, but distinguished by his own name, as "Magendie's Solution." An alternative formula is also given in which 16 grains of acetate of morphine are directed to be dissolved in two drachms of diluted acetic acid, P. L. and 6 drachms of distilled water, the reason given being that the former solution is unstable from deposition of the morphine. It is probable that this same defect was later found also in the product made by the alternative methods, for formulas of later years called for 16 grains of Morphine Sulphate dissolved in 1 fluid ounce of distilled water.

It is interesting here to note that a few years after the appearance of Magendie's Formulary the U. S. P. of 1831 contained a formula

for a solution of Morphine Sulphate which differed from both of the solutions proposed by Magendie, being four times as strong as the weaker and sixteen times as weak as the stronger, leading to years of confusion and undoubted loss of life through prescribing and dispensing errors.

The following prefatory note to the chapter on *Narcotine* will be found of interest:

"My researches have not led me to consider this matter as a medicine. I shall, however, give its history here, because it is one of the immediate principles of opium, and has thrown and still continues to throw, much uncertainty over the subject."

The employment here of the word "immediate" as we use the word "proximate" is curious but is in accord with the particular meaning it is intended to convey.

Under the *Extractum Opii Narcotina Privatum* (extract of Opium deprived of Narcotine) a curious editorial note is appended by the translator in commenting upon Dr. Magendie's statement that an exciting property is noted in extract of opium which is not observed in morphine.

"M. Magendie's conjecture is probably true; and as said in the translator's preface, it forms one of the most valuable properties of the isolated morphine, that the stimulating and constipating effects of opium are thus avoided. Mr. Battley ought to publish the formula for his *liquor opii sedativus*. It is beneath him as an old practicing member of the profession and really *useful* chemist, or rather druggist, to practice such a paltry concealment."

The *Extractum Opii Morphine Privatum* (extract of opium deprived of morphine), is nothing more than a preparation made from the drugs of the opium left after extracting the morphine by the process described under that substance. The author states:

"This residuum still exerted a certain narcotic property on animals and on man; a less marked one, it is true, than that of the common aqueous extracts, but sufficiently strong to make it useful in practice. \* \* \* It ought to be kept by all apothecaries who prepare their morphine."

*Iodine* is accorded quite a detailed description as to its properties and compounds. Credit is given to M. Courtois for its discovery in 1813 "from the mother waters of soda as it is obtained from sea weed." Potassium and sodium iodides are referred to as "Hydrio-

dates" of their respective elements. It is stated of them that "their solutions are still capable of dissolving iodine; thus forming an ioduretted hydriodate." Tincture of Iodine was made of a strength of 48 grains dissolved in 1 ounce of alcohol. The loss of strength which was already noted at that time in the tincture as prepared in that manner was explained as follows:

"It is to be feared also that the iodine may take up a portion of the hydrogen of the alcohol and thus be converted into ioduretted hydriodic acid." That these were days when enthusiasts went to almost any extreme in support of their views or to add to the sum total of human knowledge is shown by Dr. Magendie's statement that:

"I myself swallowed a spoonful of the tincture without further effect than a disagreeable taste, which went away by degrees after continuing several hours."

A formula for solution of Hydriodate of Potash, thirty six grains to the ounce is given as well as a formula for ointment of Hydriodate of Potash made by incorporating 29 grains of the salt with one and one-half ounces of hog's lard (a strength of about 4 per cent.).

The chapter on *Resin of the Nux Vomica* concerns itself with a discussion of the mode of preparation and uses of the alcoholic extract of the drug which is erroneously called the "resin." A formula for Tincture of Nux Vomica is given in which 3 grains of dry extract of nux vomica are directed to be dissolved in one ounce of alcohol. This preparation is less than half the strength of the present standard tincture.

Under *Strychnine* a method of separating and purifying the alkaloid is given. It is stated that:

"It is supposed that in the native state the strychnine is in union with a new acid, called by M. M. Pelletier and Caventou, Igasuric Acid from the Malay name of the St. Ignatius Bean." The dose of strychnine is given as one-twelfth to one-eighth grain. Formulas are given for strychnine pills containing one-twelfth grain of the alkaloid to each pill, and directing the pills to be silver coated to keep them from sticking together, the excipient and vehicle being conserve of roses. The translator adds in commenting upon this:

"We are accustomed to prevent pills from sticking together by rolling them in licorice powder or magnesia or flour; the old plan of

gilding and silvering pills is very inconvenient, for, if it be perfectly done, the pills will be effectually preserved from the action of the stomach."

A tincture of strychnine is directed to be prepared of a strength of three grains to the ounce, and a mixture of strychnine which is a suspension of the alkaloid in sweetened water of the strength of one-half grain to the ounce.

*Emetine* is directed to be prepared, as may be expected, from *ipecacuana*. An emetic mixture of emetine of a strength of nearly two grains to the ounce in sweetened orange flower water is described. Pectoral Lozenges of *Emetine* containing about one-seventh grain of emetine in each dose are described as are also Emetic Lozenges of *Emetine* containing over one-half grain each of the alkaloid. A Syrup of *Emetine* containing sixteen grains of emetine to the pound is also directed.

Another and purer form of emetine is also described and formulas given for preparations containing it in which one-fourth as much is directed to be taken of the pure *Emetine* as was directed in the corresponding preceding preparations.

*Cytisine* is a poisonous vegetable principle from the seeds of the *Laburnum*. No medicinal properties or uses are given.

*Quinine* and *Cinchonine* take up about twenty pages of the work. The species of *cinchona* mentioned are *C. cordifolia*, *C. condaminea* and *C. oblongifolia*; none of these species are recognized by the Pharmacopoeia of to-day. Methods for preparing these alkaloids are described, the cinchonine being obtained from the mother liquors after separating the quinine.

The percentage composition of quinine as given does not compare as favorably with modern figures as does that of morphine, due undoubtedly to the mixture of alkaloids which was then known by the same quinine.

	Composition as Given by Magendie. Per Cent.	True Composition. Per Cent.
Carbon.....	73.80	74.00
Nitrogen.....	13.00	8.90
Hydrogen.....	7.65	7.40
Oxygen.....	5.55	9.90

There were two sulphates of quinine described, one called *Quinine Super Sulphate* (acid sulphate of quinine). The other was

simply called Quinine Sulphate. These correspond to our present day bisulphate and sulphate, respectively.

The following formulas were proposed for the administration of these alkaloids:

Syrup of Quinine, thirty-two grains to the pound.

Wine of Quinine, twelve grains to the litre.

Tincture of Quinine, six grains to the ounce.

Syrup of Cinchonine, forty-eight grains to the pound.

Wine of Cinchonine, eighteen grains to the litre.

Tincture of Cinchonine, nine grains to the ounce.

Under *Veratrine* we find a confusion of fact and error. This "new alkali" is stated to exist in the seed of *Veratrum Sabadilla* (which is correct), and in white hellebore (which is incorrect, although excusable), and in *colchicum* (which is a startling and inexcusable error). The only method for its preparation, however, is that from *Sabadilla* seeds, although some space is given in this chapter to the therapeutic effects of *colchicum*.

*Hydrocyanic Acid* or *Prussic Acid* is described both as to its properties and its mode of preparation. Formulas are given of preparations for its administration and use. Among these are:

*Mistura Acidi Hydrocyanici* (Melange pectoral—Magendie)

Medicinal Prussic Acid.....	1 gros (59.07 grains troy)
Distilled Water.....	1 lb. (15 oz. 6 dr. 1 grain troy)
Pure Sugar.....	1½ oz. (11 dr. 10 grains troy)

Dose—One dessert spoonful.

*Potio Acidi Hydrocyanici* (potion pectoral—Magendie)

Infusion of Ground Ivy.....	2 oz. (1 oz. 7 dr. 45 grains troy)
Medicinal Prussic Acid.....	15 drops
Syrup of Marshmallows.....	Z oz. (7.52 dr. troy)

Dose—One dessert spoonful.

*Syrupus Acidi Hydrocyanici* (Hydrocyanic Syrup)

Clarified Syrup.....	1 lb. (15 oz. 6 dr. 1 grain troy)
Medicinal Prussic Acid.....	1 gros (59.07 grains troy)

The medicinal Prussic Acid above directed is described as being made from absolute HCN, by diluting it with 8.5 times its weight of distilled water. This produces an acid of about ten per cent. strength, which is stated to be of greater uniformity of strength than that produced by Scheele's process which, however, is not described but is mentioned as being usually of about half the strength of the author's. The curious precautionary note is attached to all of the

above formulas for preparations that: "It is necessary to shake the mixture every time it is used, lest great inconvenience arise from the acid being accumulated on the surface."

*Solanine* is described as being obtained from *Solanum Nigrum* and *Solanum Dulcamara*. It is stated to produce vomiting and sleep but that it had not yet been employed as a remedy in disease.

*Atropine* is stated to have been discovered in belladonna by Brandes, a contemporary and co-worker of Vauquelin, who is also stated to have discovered *Daturine* in stramonium and *Hyoscyamine* in henbane. It is stated of atropine that:

"When M. Brandes was experimenting on this alkali he was obliged to desist in consequence of violent headaches, pains in the back, and giddiness, with frequent nausea, which the vapor of atropine occasioned; it had, indeed, so injurious an effect upon his health that he has entirely abstained from any further experiments, and no one has hitherto repeated them. \* \* \* Even the vapor of the various salts of atropine produces vertigo. \* \* \* When he tasted the salt of atropine the dilatation of the eye followed to so great a degree that it persisted for twelve hours and was not influenced by the different shades of light."

*Delphinine* is described as having been separated from stavesacre seeds by M. M. Fenuelle and Lassaigue in 1819. It had not been used as a medicine.

*Picrotoxine* is credited to Boullay for its discovery and is described as being alkaline in character, a statement not in agreement with the fact as we know it.

*Gentianine* is also described as a vegetable alkali and M. Henry and M. Caventou are stated to have discovered it simultaneously and independently. This calls for the following comment from the author:

"This fact is doubly remarkable—first, because it proves how perfect the means of analyzing vegetables have become; and, secondly, because it shows the change which the progress of science has made in those who follow scientific pursuits. One hundred years ago, such a coincidence would have produced a violent quarrel, whilst now it only induces a feeling of joy in those who find their discoveries confirmed by others."



If the author had looked ahead one hundred years he might have been somewhat depressed. Such simultaneous discoveries to-day would probably result in patent right litigations.

*Lupuline* is credited to several investigators for knowledge concerning its existence in hops. Among these is the only American mentioned in the book: M. Ives, of New York.

*Brucine* was first isolated by Pelletier and Caventou from false *Angustura* bark, but Pelletier later discovered it in *nux vomica* in association with strychnine. It is stated to be an "organic salifiable base." Its properties are described as being those of strychnine in a milder degree and the statement occurs:

"It is for experience to decide whether this new substance should be preserved as a medicine or rejected."

In the posological table under *atropine*, *delphinine*, *daturine*, *hyoscyamine*, *narcotine*, *picrotoxine* and *solanine* it is stated that the dose had not yet been determined.

Credit for appendix number one is given to "Snyder's Examinations." This portion of the book comprises about fifty pages and contains methods for preparing the following classes of compounds: Acids, alkalies and their salts, earths and their salts, metals and their salts, vegetable drugs and their preservation, gum resins, expressed oils, distilled oils, distilled waters, infusions, mucilages, decoctions, extracts, mixtures, spirits, tinctures, wines, vinegars, honeys, syrups, confections, powders, pills, animal drugs, preparations of ether, plasters, cerates, ointments, liniments and cataplasma."

This is really a condensed kind of pharmacopoeia in which formulas and brief methods are given for preparing several hundred medicinal preparations. This portion of the book concludes with a table of strengths of preparations of opium, antimony, arsenic and mercury.

Appendix number two concerns itself with a twenty-page description of poisons of various kinds and their antidotes. Tests are given under some of the metallic poisons for their detection. Some of these are similar to those described in works on toxicology of to-day. Under vegetable poisons (alkaloids) the translator, who is responsible for the appendices, says:

"We are possessed of no tests by which we can distinguish poisons of this class and can only conjecture they have been taken by their taste or smell, and the symptoms."

In appendix number three there is a short discussion of the general principles of prescribing medicines, followed by typical examples of prescriptions of various kinds.

To show the prevalence of prescribing narcotics in this period of nearly a century ago it is surprising to see that out of seventy-seven examples of prescriptions, seventeen, or nearly one-quarter of the total number, call for opium or some preparation thereof.

It is interesting also to note that the translator has not ventured to make use of any of the "new remedies" described in the main portion of the work in his prescription examples.

It is both pleasant and profitable sometimes to wander through "quaint and curious volumes of forgotten lore." In the case of Magendie's *Formulary* our journey ends with a realization that the workers of that time, although poorly equipped, both as to fundamental facts and apparatus, were giants in achievement and it is for us to sincerely say, "Give us the hearts of our fathers of old."

DEPARTMENT OF PHARMACY,  
PHILADELPHIA COLLEGE OF PHARMACY.

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## CLAY AS A MEDICINE.

BY C. B. LOWE, M.D.

In the "Book of Books" are interesting references to clay. In the Book of Job (supposed to be the oldest book in the Bible), Job speaks of it as a building material, when he says, "I also am formed out of the clay," and in the 10th chapter, 9th verse he also says, "remember I beseech thee, that thou hast made me as the clay." Its tenacity is referred to in Psalm 40:2, where it speaks of the miry clay.

It is also referred to as an external application in the Gospel of John 9:6, where Christ anointed the eyes of the blind man with clay, sending him to the Pool of Siloam. It says, "he went his way and washed and came seeing." In this case the value of the application was physiological, to stimulate the man's faith.

In Wycliffe's translation of the Bible, he speaks of "rushes glewed with glewish clay and pitch" as the material with which the mother of Moses made the ark in which she consigned her infant son to the river Nile. As a side remark, the statement has recently

been made, that an official of the Standard Oil Co., reading in the Book of Exodus of the ark made from bulrushes daubed with slime and pitch, was inspired by it to prospect for oil on the banks of the Nile; it is reported as having been found in paying quantities.

We also read in the Book of Exodus of the Children of Israel, then in bondage to the Egyptians, being required to make a certain number of bricks per day, straw being furnished them as a binding material, for the clay of Egypt contains considerable sand. Finally to make their tasks harder, straw was refused them, and they were required to glean the straw from the fields, but the tale of bricks required of them was not diminished.

Clay was also used for seals, the jars of Egypt were sometimes sealed with clay, and mummy pits were also sealed with this substance, the remains of which is often found adhering to the door jambs. It is quite probable that the tomb in which the body of Christ was laid after the crucifixion was sealed with a clay seal. The seal used for public documents was rolled on the moist clay and afterwards placed in the fire and baked. It is said by Wilkinson "the sealing of doors" with clay to facilitate detection in case of malpractice is still common in the East. Before going farther it would be well to seek a definition of the word clay. The Century Dictionary says "it is the material resulting from the decomposition and consequent hydration of the feldspathic rocks, especially granite and gneiss and of the crystallin rocks in general." The National Dispensatory gives us a sharper definition, in which it says, "clay is essentially a hydrated aluminum silicate, and that the purest forms are kaolin, fullers earth and porcelain clay."

It is stated that in some parts of the earth, notably in some of our Southern States, it is a practice to eat what is called dog clay, or clay stone, the persons following this abnormal practice being generally lean and cadaverous. According to Dunglinson those who practice earth eating are called "geophagists," and the act is called "geophagism."

In trying to substantiate the above statement I came across an article in the *American Architect*, Vol. 23, page 214, by Dr. Frank H. Getchell of Philadelphia. The doctor went on a gunning expedition to Salisbury, N. C., in 1888. "In the wild hilly country back of the town he met the 'clay eaters,' a miserable race of beings with only enough energy to eke out a miserable existence. The soil is of a heavy clayey nature, but there are strata of clay heavier

than the rest. In the spring, torrents rush down from the high hills, form this clay into pellets, and rolls that accumulate in the valleys below, these are eagerly sought for and eaten." He states that he entered a cabin where a boy was crying, tied to the leg of a table; the mother stated that the boy wanted to go out and get some clay to eat, but she thought (although a clay eater herself) that he ought to eat some food first, of which there was plenty on the table. The doctor brought some of the clay home to Philadelphia and analyzed it with the aid of a friend, when it was found to contain arsenic.

In the *Literary Digest* of 1916, page 1027, is an interesting article, "Earth as a medicine and food." Some of the statements are as follows: "In the upper parts of Italy, Styria in Austria, and in certain parts of Germany the workmen butter their bread with a fine article of clay nicknamed 'stone butter.' The real home of earth eating is stated to be Asia. The famous earth of Nishpur, Persia, is used either raw or roasted, prepared with spices or perfumes. In the markets of Calcutta burnt clay is offered in small disks, the women being the principal consumers. In Africa along the shores of certain rivers in Senegambia, they use a soft soapy clay as butter. The natives of New Caledonia eat a ferruginous clay, either fresh or preserved in the form of dried perforated cakes for their dessert.

"In the neighborhood of Ouro, Bolivia, S. A., is found a white extremely delicate clay which is sent to the neighboring markets and eaten preferably with boiled potatoes.

"The ultimate reason for this dietic curiosity are manifold, the agreeable salty taste, and a perversion of the appetite being some of them. Sometimes it is the medicinal instinct, the craving for these peculiar substances is mainly a tropical instinct. This may explain the use of earth as a medicine by some of the greatest physicians of antiquity."

*Current Literature* published an article in 1902 taken from the *St. Louis Post Despatch*, entitled "The Dirt Eaters of St. Louis." It says "the dirt eater is peculiar about what dirt he eats, the article of his peculiar diet is technically a sand. It comes from the river bottoms and is made up of many little particles of granite, marble and flint, rounded with age. The chief dirt eater, Wm. Windsor by name, who is fat and jolly, has the sand collected and sterilized and distributes it among his followers at 25 cents a sack." It

seems to me that there is something of value in the claims of the health giving properties of this dirt. We all know that many dyspeptics suffer from constipation because there is no "roughage" in their food. It is asserted that much of the ill health of the Indian tribes on the Government reservations, is due to the Government issuing to them as rations, fine wheat flour, so different from the coarsely comminuted maize used by the Indians when running wild. The coarse grain containing so many indigestible particles stimulated the peristaltic movements of the bowels and constipation was unknown.

As to the use of clays as medicines we learn from the very interesting translation of Schelenz writings by Mr. Raubenheimer published in the *AMERICAN JOURNAL OF PHARMACY*, March, 1909, "that Dioscorides taught that alum possessed healing and astringent properties, that it cured boils and carbuncles, frost bite, etc.

"In ancient times, earths got the reputation of being remedies against poisons and also against plague or contagious diseases.

"The ancients went so far as to claim that the dishes and vessels burned from these clays and earths also possessed medicinal properties, inasmuch as they transferred magic power to the liquids contained therein. Red clays were also very popular, Bole Armenia was especially renowned as a remedy against plague.

"Many family recipes, handed down for centuries involved the use of various earths, externally applied as clay poultices for bee stings, ulcers, sores and all kinds of inflammations."

Thos. Keenan in an interesting article in the *American Druggist*, February, 1914, says that "Antiphlogistine which was placed on the market in 1893 was an impure form of kaolin, originally mined in Wyoming, now obtained from other sources. The name kao-lin is of Chinese origin, meaning high hill in allusion to a high hill in the neighborhood of the chief ceramic town in China."

We find that clay in various forms has been used as a medicine for generations, either externally or internally, its value probably residing in its powers of both absorption and adsorption. When used as a poultice its heat and moisture tend to soften and relax the tissues, thus relieving pressure upon the nerves and also taking up discharges from suppurating wounds, sores, etc.

"Prof. Una of Hamburg, a renowned dermatologist, holds that the therapeutic action of Cataplasma Kaolin is due chiefly to the glycerin, and others have expressed similar opinions. Una contends

that by increasing the sensible watery vapor the cataplasm causes an increased flow of water to the superficial tissues, and the serous soaking causes their softening. This may be, but he has overlooked the power of adsorption possessed by the kaolin in addition to the extraordinary power for absorbing water, it may be supposed to have great selective action in absorbing the secretions of the tissues. It is well known that clays are capable by adsorption of removing solid substances from solutions with which they come in contact, these bases and substances being held so that they can not be washed out again;" for this reason Prof. Fantus of Chicago, asserts that it is an effective antidote in strychnine poisoning. For pharmaceutical purposes kaolin should be treated with 5% of hydrochloric acid to remove lime, and afterwards levigated to remove sand. As it is free from organic matter it is an excellent excipient for making pills of potassium permanganate and silver nitrate.

The Cataplasm of Kaolin is a better preparation than originally introduced because both kaolin and glycerin are thoroughly heated to expel moisture.

According to the U. S. P., "clay has been used internally as a remedy in Asiatic Cholera, gastro-enteritis and dysentery, its effects in the latter condition are largely those of a protective."

According to Dr. Hess it surpasses either bismuth or chalk in lessening diarrhoea.

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A MORE EFFECTIVE AND ECONOMICAL BASE FOR THE  
APPLICATION OF MUSTARD OIL, THAN THE  
OLEAGINOUS BASES HERETOFORE EM-  
PLOYED.

BY GEORGE E. ÈWE,

PHILADELPHIA, PA.

Dr. Torald Sollman, of the Pharmacological Laboratory of the School of Medicine, Western Reserve University, recently published an article in the *Journal of Pharmacology and Experimental Therapeutics* (Volume XI, 1918, pages 229 and 30), entitled "Cutaneous Irritation by Mustard Oil as Influenced by Various Solvents."

In that article, Dr. Sollman reported that the various vehicles for the mustard oil, which he tried, possessed irritant efficiencies in 1 per cent. solutions or suspensions in the following order:

1. Olive Oil	}	Practically no hyperemia.
2. Turpentine		
3. Ether	}	Very little hyperemia.
4. Absolute Alcohol		
5. 95% Alcohol	}	Marked and lasting hyperemia.
6. 50% Alcohol		
7. Mucilage of Acacia	}	Most intense and persistent hyperemia.
8. Simple Syrup		

The purpose of this note is to suggest an aqueous vehicle which is of more convenient consistency than mucilage of acacia or simple syrup. The vehicle which I wish to suggest is an aqueous 3 per cent. tragacanth paste.

This vehicle is made by soaking 3 parts of ribbon tragacanth and 97 parts of water together, with occasional agitation, for 24 hours, or until the ribbons are completely expanded. The paste is then squeezed through a piece of cheese cloth to remove obvious solid particles, if necessary. The paste, so made, is of ointment-like consistency and can be readily spread or rubbed on the skin.

The mustard oil can be readily incorporated with this vehicle by whipping it in with an egg beater (preferably of the covered type to prevent loss of oil and also annoyance to the operator). A covered emulsifier is also well adapted to the incorporation of the oil.

The mustard oil strength of the application is a matter for individual preference, based upon the effect desired and the length of time it is desired to allow the application to act. The average commercial mustard oil application, made with an oleaginous base, usually contains about 3 per cent. of mustard oil. Most pharmaceutical manufacturing companies list such a product. Therefore, a mustard oil application made with an oleaginous base and containing 3 per cent. of mustard oil was taken as a standard for the strength of mustard oil application, with which the trade is familiar, and this application was compared with mustard oil applications made with 3 per cent. tragacanth paste and containing various proportions of mustard oil, in determining the relative irritation efficiencies of the two types of bases.

The standard application with oleaginous base was made with a base consisting of 15 per cent. of paraffin and 85 per cent. of yellow petrolatum.

Repeated comparative irritation experiments, when made upon the shaven abdomens of guinea pigs, led to the conclusion, that, in general, a 2 per cent. mustard oil application made with tragacanth base, ably represented in irritation efficiency, a 3 per cent. mustard oil application made with a base composed of paraffin and yellow petrolatum.

The keeping qualities of the application made with tragacanth base are excellent provided the container is kept hermetically sealed; the collapsible tin tube being the logical container for this application.

PHARMACEUTICAL RESEARCH LABORATORY,  
H. K. MULFORD COMPANY,  
PHILADELPHIA, PA.

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### THE COMPOSITION OF SALVARSAN.

At a meeting of the Chemical Society on March 18, a communication from the Wellcome Chemical Research Laboratories on the composition of salvarsan by Professor F. L. Pyman and Mr. R. G. Fargher was read by the latter. Commercial salvarsan prepared by the reduction of 3-nitro-4-hydroxyphenylarsinic acid by means of sodium hyposulphite, solution of the 3 : 3<sup>1</sup>-diamino-4 : 4<sup>1</sup>-dihydroxyarsenobenzene so obtained in methyl alcohol containing hydrogen chloride, and precipitation of the salt by means of ether, is generally regarded as 3 : 3<sup>1</sup>-diamino-4 : 4<sup>1</sup>-dihydroxyarsenobenzene dihydrochloride containing combined solvent. The latter according to the earlier work of Ehrlich and Bertheim, is methyl alcohol, and it has been suggested recently by Kober that the variable toxicity of salvarsan can be accounted for on this assumption. On the other hand the circulars of the first makers, the Farbwerk vorm. Meister, Lucius u. Brüning, suggest that the combined solvent is water. It has now been shown that the retained solvent consists almost entirely of water, support for the view being adduced from the elementary analysis of salvarsan and direct estimation of methyl alcohol, the amount present varying from nil to 1.4 per cent. The replacement of ether by acetone in the precipitation leads to a product, which, in addition to the customary solvent which can be removed in a vacuum, contains a molecular proportion of acetone.

<sup>1</sup> A contribution from The Wellcome Chemical Research Laboratories, London, Eng.



It was originally indicated by Ehrlich and Bertheim that the crude base from the hyposulphite reduction contained sulphur attached to arsenic which was removed by conversion into the hydrochloride. The authors found, however, several years ago, that commercial salvarsan of both British and German origin invariably contained sulphur, the amount varying generally from one to two per cent. (compare Medical Research Committee, Special Report Series No. 44, Reports of the Special Committee on the Manufacture, Biological Testing and Clinical Administration of Salvarsan, No. 1, p. 8). As the result of a comprehensive series of experiments it was concluded that at least a portion of the sulphur was present in acidic form, most probably as a sulphaminic acid,  $R.NH.SO_3H$ , and a product closely approximating in composition to the hydrochloride of the monosulphaminic acid of salvarsan,  $(HCl, NH_2)(OH) C_6H_3.As_2.C_6H_3 (OH) (NH.SO_3H)$ , was actually isolated. The presence of this product, which could be estimated quantitatively with some degree of accuracy, did not as a rule account for the whole of the sulphur, and evidence was given in support of the assumption that a proportion of the remainder was attached to arsenic. It was also suggested that owing to the fact that salvarsan possessed some of the properties of a colloid sulphur might be present merely in physical association. The last section of the paper dealt with the preparation of pure diamino-dihydroxy arsenobenzene dihydrochloride, the most satisfactory process being the reduction of 3-amino-4-hydroxyphenylarsinic acid with hypophosphorous acid. It is interesting to record that a specimen of this pure material tested by the Medical Research Committee proved to be more than normally toxic.

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### FORMOSA, THE HOME OF CAMPHOR.

The March, 1920, issue of the *National Geographic Magazine* contains a profusely illustrated article on "Formosa the Beautiful," by Alice Ballantine Kirjasoff, in which an interesting account is given of the camphor production of this isle whose "plateaus covered with camphor laurel, are the largest tracts of these valuable trees in the world." The information contained therein that is considered of especial interest to the student of drug products is presented to our readers in this abstract:

The population of Formosa is mainly agricultural. The cultivation of rice, and more especially sugar-cane, is encouraged by the government, and these are grown in great quantities. However, the most interesting industry is the production of camphor, and it can be truly said to be peculiar to the island, when it is remembered that Formosa holds a practical monopoly in the world's market of this valuable drug. Before the war, Germany, by a secret process, succeeded in manufacturing some synthetic camphor, but so expensive was the labor entailed, that the artificial product could not compete with the natural camphor, nor is it likely to do so for some time to come.

Shortly after the Japanese came to Formosa, 25 years ago, the camphor industry became a government monopoly. Before that time there had been a great deal of ruthless waste, both in the cutting down of trees and in extracting camphor from them. At first, the Japanese, too, were careless in this respect, for the supply of camphor trees seemed practically limitless, but the great increase in the demand for the product in late years has made scientific afforestation necessary. Now large tracts of land are given over to the cultivation of the camphor laurel. The oldest trees are now twenty years of age and these, I am informed, are to be cut down next year.

According to an article appearing recently in a semi-official publication of Formosa, the camphor produced in the island at the present time is obtained entirely from natural grown camphor trees, the supply of which, it is anticipated, will be exhausted within ten years. For more than a decade, however, the camphor monopoly bureau had been planting camphor trees at the rate of more than 3,000 acres a year. In 1919 its program was expanded to more than 12,000 acres, and this will be the annual acreage planted in the future. In recent months the demand for Formosa camphor has been exceedingly heavy, especially among celluloid manufacturers. For the first three months of 1920 the Japanese Government has allotted to the United States 379,635 pounds.

Paradoxically as it may seem at first glance, the savage head-hunters of Formosa have been both an impediment and a boon to the camphor industry. As the forests are cut down, the head-hunters have to be driven further back into the mountains. These expeditions against the savages are never very successful, encountering as they do heavy obstacles in the way of dense forests, rapid streams without bridges, steep mountains without trails, and above all, the danger of sudden attack.

The life of a camphor worker is indeed an adventurous one; he is never safe. Although a woodman with an axe never moves except in the company of an armed guard, there is always danger of an ambush. Tales of the camphor workers recall the days of our pioneer fathers in the times of the tomahawk, the poisoned arrow, and the scalping knife. And yet if this menace had not existed, the camphor forests would have disappeared long ago. Thanks to the head hunters, there are still large tracts of virgin camphor forests in Formosa.

Camphor trees grow best on moderate, well drained slopes, not over 4,000 feet in elevation, where the sun's rays can reach them. Nowhere else in the world have these trees attained such height and girth. In the past, trees with a basal circumference of from 30 to 40 feet have been noted, but these have inevitably fallen victims to the woodman's axe. Perhaps in the uncharted forests, where the savage still holds sway, more of these noble specimens still grow unscathed. At present a camphor tree with a basal circumference of 20 feet is considered a very ample specimen.

In the point of view of value, few trees can rival the camphor. An average tree, say with a basal circumference of 12 feet, will yield about 50 piculs of camphor (approximately 6,660 pounds), which, at present market price, is worth about \$5,000. Strictly speaking, there are no camphor forests, as the camphor laurel is only one of a number of trees growing together. The camphor trees are unusually beautiful, with shapely trunks and wide-spreading branches profusely covered with graceful leaves of a soft green.

Native stills are scattered here and there throughout the districts where crude camphor is collected, packed in tins and carried down precipitous mountain paths on coolies' backs to the nearest railway line, whence it goes to the refinery at Taihoku.

The still we visited was operated by the members of one Chinese family. When our party approached, some of the men were gouging chips from the trunks of camphor trees with adzes, while others were in the still feeding the fires. Adjoining the still was a shanty, where the workers lived, and in front of the door was a woman preparing the afternoon meal, while beside her a little boy was busy playing blocks with chips from which the camphor had been extracted. The stills are operated in a very simple manner. Camphor chips are placed in a chip retort over boiling water, and as the camphor vaporizes it passes through pipes into submerged vats, which are so

arranged that cool water from a mountain stream can run over them to accelerate crystallization. After the camphor has crystallized the vats are opened, and the product is placed on wooden troughs to allow whatever free oil there may be to drain off. This oil will yield 90 per cent. of crude camphor in the process of refining.

## THE FAT OF MOMORDICA SEEDS.\*

By C. E. CORFIELD, F.I.C., AND E. CAIRD, B.Sc., A.I.C.

At the request of the Assistant Director of the Royal Botanic Gardens, Kew, an examination of the fat contained in the seeds of *Momordica cochinchinensis* (Spreng.) was undertaken with the view to ascertaining whether it might prove of commercial value.

*Momordica cochinchinensis* is a cucurbitaceous plant indigenous to Bengal, Tenasserim, the Deccan Peninsula, Formosa, and the Philippine Islands. The seeds are described by Hooker as "7/8"  $\times$  5/8" and 1/5" thick, many, horizontal, irregular, ovate, compressed, black, corrugated on the margins, sculptured on the faces." (*Flora of British India*, 2: 618.)

Very little information has been published concerning the fat of these seeds. In the *Pharmacographia Indica* (2: 77) the statement is made that the seeds yield to light petroleum ether 43.74 per cent. of a slightly greenish oil, which smeared on a glass plate and exposed to a temperature of 100° C., could be scraped off the glass as a white powder, which, when boiled with petroleum ether, yielded only a trace of oil.

A general examination of the seed-coats and kernels has been made by Greenish and Baines, with the following results:

The average weight of each seed was 3.13 Gms., of which the seed-coat weighed 36.7 per cent., and the kernels 63.3 per cent.

### A.—SEED-COATS.

The powdered seed-coats were extracted successively with different solvents, the solvent evaporated, and the residue dried at 100° C.

	Per cent. of Seed-Coat.	Per cent. of Seed.
1. Petroleum Spirit Extract.....	0.33	0.12
2. Ether Extract.....	0.16	0.06
3. Chloroform Extract.....	0.44	0.16
4. Alcohol Extract.....	1.62	0.59

No alkaloid was found in any of the residues.

\* From *The Pharm. Jour. and Pharmacist*, January 17, 1920.

## B.—KERNELS.

	Per cent. of Kernel.	Per cent. of Seed.
1. Petroleum Spirit Extract.....	47.06	28.90
2. Ether Extract.....	1.03	0.65
3. Chloroform Extract.....	0.17	0.11
4. Alcohol Extract.....	3.44	2.18

Again it is interesting to note that no alkaloid was present in the residue. The residue from the petroleum spirit extract was a pale brown viscous oil. On exposure to air it rapidly filmed on the surface, and on continued exposure it was converted into a whitish solid mass, easily reducible to a powder.

The result of these experiments led to the present examination of the seeds with a view to ascertaining whether the oil would be of commercial value as a drying oil.

Since, as will be shown later, the heating of the oil to a temperature approaching  $100^{\circ}$  C. had the effect of altering the composition of the oil, a method, other than that of extraction by means of a solvent and subsequent evaporation, was employed. Cold compression yielded little, since the fat was fairly solid. With the application, however, of slight heat the fat was readily yielded, and a method of extraction based upon this result was adopted. After removal of the seed-coats the kernels were coarsely powdered and submitted to pressure, the necessary heat being obtained by means of a steam coil round the press, and was adjusted to produce in the mass a temperature of about  $40^{\circ}$  C. The fat, of which a good yield was obtained, was greenish brown in color; had an unpleasant and penetrating odor; on cooling, solidified to a pale green, granular mass; when worked at atmospheric temperature became fluid. The green color was most probably due to traces of chlorophyll from the coating of the cotyledons.

On examination the fat gave the following constants:

Saponification value.....	185.2
Acid value.....	1.9
Iodine value.....	23.4
Refractive index ( $40^{\circ}$ C.).....	1.496
Ester value.....	183.3
Melting point.....	$28^{\circ}$ C.— $32^{\circ}$ C.
Unsaponifiable matter.....	a trace

After saponification of the fat the alcohols were separated, and were found to consist principally of glycerol, the residue giving no

evidence of the presence of wax-alcohols. The fatty acids on separation were found to be yellowish brown in color and solid. The following constants were observed:

Melting point.....	46° C.-51° C.
Solidifying point.....	44° C.-42° C.
Acid value.....	188.3
Iodine value.....	about 40

Since some considerable difficulty was encountered in determining the iodine value, the figure is not taken as final. Apparently the absorption is accompanied by the formation of some unstable compound, which is decomposed by sodium thio-sulphate. From these constants it appears that the fat consists chiefly of the glyceryl esters of fatty acids, the larger portion of which are saturated, but no attempt has been made to determine the composition of the fat.

On exposing the fat to the atmosphere a change in color and in form was noticed. The fat gradually lost its green color; assumed a pale yellow shade; a marked tendency for films to agglomerate was apparent; finally it became granular in appearance. A systematic examination of these films was conducted with a view to determining the cause of these changes.

The following tables will show the course of the experiments:

A.—3.9536 GMS. EXPOSED TO AIR AND LIGHT.

Time of Exposure in Days.	Actual Gain. Gm.	Gain per Gramme per Day. Gm.
1.....	0.0024	0.00061
2.....	0.0070	0.00177
3.....	0.0216	0.00546
4.....	0.0312	0.00789
5.....	0.0505	0.00425

These figures are no measure of complete change, since, owing to agglomeration, the lower layers were not sufficiently exposed.

B.—3.5913 GMS., EXPOSED TO AIR, WITHOUT ACCESS OF LIGHT.

Time of Exposure in Days.	Actual Gain. Gm.	Gain per Gramme per Day. Gm.
1.....	0.0003	0.000835
2.....	0.0011	0.003063
3.....	0.0025	0.0006961
4.....	0.0074	0.002060
7.....	0.0082	0.000761

In this experiment there was no agglomeration, and the only change in form was the appearance of small, white points in the green exposed surface.

C.—3.9894 GMS., EXPOSED TO LIGHT IN NITROGEN.

For a period extending over seven days no change in weight took place.

From the above figures it is evident that the change observed is one of oxidation, which is immensely accelerated by the presence of light, since in that experiment in which the fat was excluded from light the change was extremely small, and only affected the most exposed portions. The effect that this oxidation has upon the solubility of the fat in the ordinary solvents was next ascertained. The data are tabulated below, and will again show that there was practically no change when the fat was kept in the dark:

	Petroleum Spirit.	Ether.	Carbon Tetrachloride.	Alcohol (97%).
Original fat.....	Soluble	Soluble	Soluble	Insoluble
Exposed in light....	Insoluble	Insoluble	Insoluble	Insoluble
Exposed in dark....	Faintly opal- escent solution	Faintly opal- escent solution	Faintly opal- escent solution	Insoluble

Lastly, the effect of heat upon the appearance and properties of the fat was observed.

A.—3.5712 GMS. EXPOSED TO AIR AND LIGHT AT 100° C.

Time of Exposure in Days.	Actual Gain.	Gain per Gramme per Day.
1.....	0.1912	0.05652
2.....	0.0614	0.03714
3.....	0.0140	0.00392
4.....	nil	nil

At this point the weight of the film had become constant, indicating that complete oxidation, and other change, if any, had occurred during the period of three days. The appearance of the heated film was markedly different from that of the film exposed at atmospheric temperature. The green color was lost and the fat assumed a granular, gelatinous form, of a pale brown color, finally becoming stiff, and easily disintegrated. The effect of heating during oxidation was, as in the case of oxidation at ordinary temperatures, to render the product insoluble in the fat-solvents, petroleum spirit,

ether, and carbon tetrachloride, while it remained insoluble in alcohol.

The following is a record of observations made on heating the fat slowly from 15° C. to 240° C.:

15° C.—50° C.—The fat became less granular, finally assuming a homogeneous appearance, and was of a dark brown color.

50° C.—100° C.—No change observed, except that the other color assumed a redder tint.

100° C.—110° C.—More transparent.

120° C.—130° C.—Color still lighter.

130° C.—180° C.—Appearance of small bubbles, probably due to the escape of a small quantity of volatile matter.

200° C.—240° C.—A greenish brown mobile liquid.

On cooling, the fat remained as a brown viscous liquid of the consistency of castor oil, and the solubility remained as that of the original fat. On exposure in thin layers this liquid did not exhibit the character previously recorded of the fat. During two days no film appeared, whereas on further exposure the thinnest portions formed a transparent skin of the nature of a varnish.

In conclusion, the evidence is that the fat shows certain characteristics of drying oils, such as Tung oil, without the property of producing a varnish, as is the case with drying oils, such as Linseed oil, whereas after heating it behaves as a semi-drying oil, and it would seem that in this condition, admixed with drying oils, it might be used in the production of paints and varnishes.

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## THE ASSAY OF IRON FILINGS FOR PHARMACEUTICAL USE.\*

BY H. HINDLEY, PH. C.

Iron in the form of fine filings, though not official in the B. P., is frequently used in the manufacture of medicinal preparations containing iron, instead of nails or wire, and as it is more liable to contamination in this form, it demands more careful examination. From a medicinal point of view its actual content of metallic iron

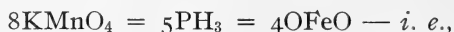
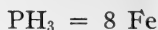
\* From *The Pharm. Jour. and Pharm.*, Feb. 7, 1920.



is not so important as in ferrum redactum, which depends for its medicinal properties on the metallic iron it contains. It is necessary however, that it be nearly pure, as the presence of much oxide would seriously alter the iron content of the preparation if allowance were not made. An estimation of its iron content, both free and combined, is therefore necessary.

Iron filings are official in the German Pharmacopoeia as ferrum pulveratum, but the assay process therein given estimates the total iron only, whether free or in any state of oxidation. The proportion of free metallic iron may be estimated by the official B. P. method for ferrum redactum, by allowing the filings to react with copper sulphate solution and titrating the ferrous sulphate thus formed with potassium permanganate. In using this process for ferrum redactum, it has been pointed out by Peck (*Year-Book of Pharmacy*, 1898, p. 399), that it is difficult to secure accurate or even concordant results unless certain experimental details be adhered to. This lack of concordance is due chiefly to the incompleteness of the reaction, in varying degree, due to the formation of a protective coating of metallic copper on the iron particles, and to the massing together of the particles, preventing the reaction proceeding with sufficient rapidity to be completed in the specified time. These objections apply to filings also, with greater force if they are somewhat coarse, and if care is not taken results may be obtained which are below the truth or above for a reason to be discussed. Peck directs that the copper sulphate solution be added cold to the iron, the solution heated in a flask with Bunsen valve for half an hour, then rapidly filtered and titrated. In assaying a number of samples of iron filings by the B. P. process another complication made itself evident, and the results obtained were not only inconcordant, but in some cases impossibly high, being several figures over 100 per cent. Using Peck's modification, similar results were obtained. This was not explainable for some time, till on one occasion a smell of phosphine was noticed in the hot, unacidified solution. The odor was like that of acetylene from calcium carbide. This latter smell is really due to traces of phosphine, pure acetylene being odorless. The presence of phosphine suggests the presence or formation of hydrogen, either as occluded hydrogen or formed by galvanic action between the copper and the iron, and combining while nascent with the phosphorus in the iron. The latter explanation is the more probable. As phosphine,  $\text{PH}_3$ , reacts with potassium permanganate,  $\text{KMnO}_4$ , according to the

equation:  $8\text{KMnO}_4 + 12\text{H}_2\text{SO}_4 + 5\text{PH}_3 = 4\text{K}_2\text{SO}_4 + 8\text{MnSO}_4 + 12\text{H}_2\text{O} + 5\text{H}_3\text{PO}_4$  it was considered likely that traces of phosphine (and probably some hydrocarbon) were responsible for the abnormally high results obtained. It will be seen from the above equation that



$$35 = 447$$

so that phosphine has the reducing power of about thirteen times its weight of iron; consequently, a little in the solution, if calculated as iron, would produce the high result. So little as 0.000437 Gm. of phosphine reduces 1 Cc. of  $N/10$   $\text{KMnO}_4$ . Sulphuretted hydrogen would act similarly, but the proportion of phosphorus in iron (which may be 0.7 per cent. in cast iron), judging from published analyses of iron, is from four to seven times that of sulphur. That the gas evolved was phosphine was proved by dissolving 5 Gms. iron filing in dilute sulphuric acid in a flask and passing the gas generated through a solution of potassium permanganate in another flask. The permanganate solution was then decolorized with tartaric acid and tested with excess of ammonium molybdate in nitric acid, when ample evidence of phosphate was obtained. It might be expected that if phosphine is formed it would be precipitated from the solution as copper or iron compounds. In the case of small amounts, however, and under certain conditions, such as the reducing influence to the copper-iron couple, it is possible that precipitation may not take place. It was notable that the odor of phosphine was not always perceptible, though some may have been formed in further experiments on the sample which had previously yielded it under apparently the same conditions. In fact, odor of phosphine was not the rule. Assuming, phosphine, however, to be the disturbing factor, prolonged boiling was tried to eliminate it from the solution, and this was found successful. The following process was employed:

0.025 Gm. of iron filings and 1.25 Gms. of copper sulphate were ground together in a small mortar to thoroughly subdivide the filings, then rinsed into a narrow 4,000 Cc. glass beaker with about 60 Cc. of cold water. The contents of the beaker were then brought to the boil and kept briskly boiling till reduced to about 15 Cc., then rapidly filtered, preferably at the pump, through a Gooch crucible or through a small Buchner funnel. The time of filtration is thus

reduced to a few seconds, lessening the chance of oxidation and mechanical loss. But filtration must be thorough, and no trace of precipitate must be allowed to remain in the solution, for it has a strong reducing action on the permanganate. Wash with about 100 Cc. of cold water, add sulphuric acid, and titrate as usual.

This treatment appears to get rid of the phosphine. Either it is volatilized as formed, or it is completely precipitated at the boiling temperature by the excess of copper sulphate. Brisk boiling also aids interaction by keeping the particles from massing together. There is no fear of oxidation while boiling, as, in the narrow beaker the liquid is covered with an atmosphere of steam. The originators of the process official in the German Pharmacopoeia may have had the effect of such impurities in mind when they devised the method which is as follows:

1 Gm. of *ferrum pulveratum* is dissolved in about 50 Cc. of dilute sulphuric acid and made up to 100 Cc. with water. 10 Cc. of this solution is treated with  $\frac{1}{2}$  per cent. solution of potassium permanganate, sufficient to produce a faint pink. The solution is then decolorized by means of tartaric acid, 2 Gms. of potassium iodide are added. The stoppered flask is allowed to stand one hour, and the liberated iodine is then titrated with  $N/10$  sodium thiosulphate. The iron and such impurities as phosphorus and sulphur are fully oxidized. The final oxidation products of the phosphorus and sulphur have no effect on the potassium iodide, whereas the ferric sulphate is reduced to ferrous sulphate, which liberates the equivalent of iodine. The process is required to yield 97.7 per cent. of total iron. The same process is used for *ferrum redactum*, which is required to indicate 96.6 per cent. of total iron. It must not be forgotten, however, that a standard base on the total iron is sufficient to ensure a minimum of the free metal being present when the figure approaches 100 per cent., as in the German test. But it fails to give a measure of the free metal, and is, therefore, only a check on a prearranged standard. Clearly, filings from a cast-iron at 95 per cent. or less would be rejected by the German Pharmacopoeia test, and only filings from steel or wrought iron which indicate 98 per cent. to 99 per cent. free iron are considered suitable. Such a standard determined with the precautions indicated, secures medicinal preparations with full iron content.

The work in connection with this note was carried out in the laboratory of Messrs. Evans Sons, Lescher and Webb, Liverpool.

## PURIFIED CRESOL (CRESYLIC ACID).\*

BY HERBERT C. HAMILTON,

RESEARCH LABORATORY, PARKE, DAVIS &amp; COMPANY, DETROIT, MICH.

One of the minor problems arising from the war because of interference with importations from Europe was that of obtaining a substitute or equivalent for trikresol, a proprietary article imported from Germany and extensively used as a preservative and disinfectant. As has been shown to be true in many other instances, it is equally true in this case that there is no lack in America either of crude material or of ability to purify it. There was required only the incentive.

Trikresol is so named because it is a mixture of the three isomeric cresols naturally occurring in coal tar. These three cresols are identical in composition, but have different physical and bactericidal properties. These differences, however, are unimportant and nothing of practical value results from their separation.

Trikresol, while useful as a general antiseptic and germicide, with a phenol coefficient of  $2\frac{1}{2}$  to 3, found its more extensive application as a preservative for serums, vaccines and similar biologic substances. Careful research has proved that for this purpose, with one exception,<sup>1</sup> no other antiseptic has been found entirely suitable, either because of its efficiency or the toxic or irritating action when absorbed from a hypodermic injection.

The cresols have practically the same toxicity as pure phenol, as shown in the accompanying table, but the corrosive action is so low and the germicidal value so high in comparison, that the use of phenol as a germicide is no longer logical. To illustrate: cresol with a coefficient of 3, when diluted 1 to 60, is equal in every respect to a 5 per cent. solution of phenol, while the toxicity of the solution is only one-third as great because of the degree of dilution, and the corrosive action, while not measurable with accuracy, is less than one-third as great.

Superficially trikresol is identical with the cresols of coal tar, since an average sample of the latter contains not over 5 per cent. of constituents other than the cresols. But it was very promptly observed that cresol, as it appears on the market under various

\* *J. Ind. Eng. Chem.*, Jan. 9, 1920.<sup>1</sup> Carl Voegtlin, Hygienic Laboratory, *Bulletin* 96.

names, is inapplicable for use as a serum preservative because of three specific reasons, all of which are interrelated, namely:

1. Incomplete solubility.
2. Disagreeable odor.
3. Color.

Incomplete solubility is due to the presence of one or more of three substances, naphthalene, colored compounds formed apparently at the expense of the cresols, and phenols of higher boiling point and less solubility than the cresols.

The disagreeable odor is largely due to pyridine and partly to the naphthalene which have been incompletely separated in preparing the crude phenol.

The origin of the color which appears in cresol and phenol is more or less uncertain. It is probably not always due to the same cause, but may in some cases be due to impurities in the cresol, and in others, to incidental conditions, such as the effect of light or air or the action of alkali from the glass container.

It is said that the germicidal value of a highly colored lot is greater than that of a clear straw-colored sample. This, however, is probably a hastily drawn conclusion from insufficient evidence, since different lots are found to differ much more than a water-white and a colored sample from the same lot. Redistillation corrects the color and can improve the solubility and odor, but not to a sufficient extent.

The development of color appears to be a property not only of cresols but also of pure phenol and no method has been devised by which such a change can be entirely prevented. The coloring matter appears to be a new constituent and to have properties entirely different from those of the original cresols. It remains behind on redistillation, but further quantities form so that only the freshly distilled material is entirely colorless.

Gibbs<sup>2</sup> ascribes the development of color by the action of sunlight to a labile hydrogen atom and describes experiments with the three cresols in which coloration occurred in varying times with the different ones, but all were affected in the same way.

This, however, does not explain the immediate cause of this coloration. A sample of a freshly redistilled lot was set in the sunlight and another was kept in an amber bottle in the dark. The first, after three months, was very slightly tinged with pink, the

<sup>2</sup> *J. Am. Chem. Soc.*, 34: 1190, 1912.

other was decidedly reddened. This is not an isolated case but was a careful demonstration of what frequently occurs in practice with large lots. Sufficient observations have not been made to arrive at a theory as to the cause or causes of the change and no method has consistently prevented its recurrence.

The disagreeable odor is due to pyridine and naphthalene which one would naturally think were eliminated in the process of separating the cresols from the creosote oil. In this process the acid constituents of the oil are combined with an alkali such as caustic soda or lime, and in this form should be readily separated from the neutral and basic substances. In fact only a very small percentage of these bodies remain with the cresols and are dissolved with it when its alkaline combination is broken up, as it is in practice, with carbonic or sulphuric acid. The odor of crude carbolic acid is not distinctly like either impurity, since the natural odor of the cresols masks the others until they are unrecognizable. Distillation carries these impurities over and little improvement can be accomplished by this step as the sole purifying process.

Nevin and Mann<sup>3</sup> depended on separation by redistillation to obtain the proper fraction but this, as noted above, while removing the colored and some of the insoluble impurities, fails to remove pyridine and naphthalene, which are responsible for the odor. While this odor is perhaps negligible, it is easy to detect the difference between two lots of cresol, one purified to remove the odorous impurities, as will be described later, and the other purified by redistillation only.

In my experiments an attempt was made to study the sodium cresylate compound when prepared in molecular proportions. In concentrated solution no observable separation takes place to indicate that purification by this means is feasible, but on further dilution the naphthalene crystallizes out in a well-recognized form and often in considerable quantities. This can be filtered out, but on again recovering the cresols no material improvement in odor results, because the naphthalene is the less objectionable of the two.

My next experiments were carried out having in mind the examination of sodium cresylate in solid form to see if impurities could be detected, identified, and removed by tests applied to the dried or crystallized material.

<sup>3</sup> *J. Am. Chem. Soc.*, 39: 2752, 1917.

In the process of evaporating the solution it was observed that the vapors smelled distinctly of pyridine, and further, that after a certain time no odor of this character could be detected. Carrying this experiment to its conclusion and recovering the cresols, they were found to be practically free from the objectionable odor of the crude cresols and on redistillation a water-white soluble product was obtained with no odor but that of the pure cresols.

The practical working out of this process is as follows: Dissolve the crude cresol in a solution of caustic soda molecularly equivalent, using sufficient water to dilute the sodium cresylate to a 25 per cent. solution. Then boil, or drive live steam through the solution until the odorous impurities have passed off with the steam. If the solution is boiled over an open flame, care is necessary to avoid concentrating the solution too much, as the cresylate breaks up and free cresol is volatilized and may take fire. It is important to add water to replace that lost by evaporation.

The time necessary to vaporize the impurities varies with the amount present, and can be determined by smelling. "The nose knows" when the pyridine is gone. The solution should be allowed to become cold and then observed to see if naphthalene or other neutral oils are present. Any floating oil can be skimmed off, while the naphthalene, if any remains unvolatilized, can be removed by filtration or centrifuging.

Treatment with sulphuric acid equivalent to the alkali originally used will break up the cresylate and set free cresol which can be recovered as a supernatant layer over the sodium sulphate solution. Separation should be very complete, as the water otherwise present causes trouble in distilling.

The removal of these two impurities, which rarely amount to more than 5 per cent. of the cresols, is therefore equivalent to a complete purification of the substance, since the color is automatically removed by redistillation, and a careful observation of the temperature of distillation at the end of this step insures the removal of the higher boiling phenols which are less soluble than the cresols and may for that reason be considered as impurities.

#### TOXICITY ASSAY.

Sample.....	Purified cresols
Animal.....	Guinea pigs
Method.....	Subcutaneously

CRESOL.		
Wt. of Animal.	Dose per Kilo.	Result.
0.572	0.6	Recovered
0.611	0.6	Recovered
0.577	0.7	Died
0.640	0.7	Died
0.572	0.8	Died
PHENOL.		
0.437	0.5	Recovered
0.480	0.5	Recovered
0.446	0.6	Died
0.480	0.6	Died
0.570	0.6	Died
0.340	0.7	Died

Toxicity about 90 per cent. of that of phenol: Worth Hale, Hyg. Lab., *Bulletin* 88; James Leake and Hugh B. Corbin, Hyg. Lab., *Bulletin* 110.

## GERMICIDAL ASSAY.

Sample.....Purified cresols.

Method.....A. P. H. A. phenol coefficient method.

(Committee Report, *Am. J. Pub. Health*, 8 (1918), 506.)

Organism.....*B. typhosus*.

DILUTIONS.		TIME AND RESULTS.			
Sample.	5	10	15	20	
1-300	—	—	—	—	
1-350	—	—	—	—	
1-400	+	—	—	—	
1-450	+	+	—	—	
1-500	+	+	+	+	
Phenol					
1-100	—	—	—	—	
1-110	+	—	—	—	
1-120	+	+	—	—	
1-130	+	+	+	+	
1-140	+	+	+	+	
Coefficient 3.6.					

The cost of the process is inconsiderable, since no complicated chemical or mechanical steps are necessary. It is evident from observation of the steps in the process that no unusual equipment is needed and only the commonest chemicals are employed. It is evident, therefore, that here again the German chemists profited at our expense for many years while the crude materials waited only for proper development.

The logical place for the economical production of the refined cresols is where the crude material is first separated from the oils



distilled from coal tar. These crude phenols, necessarily dissolved in alkali to separate them from the neutral oils, can, at that point, by suitable means, be freed completely from their impurities, and after fractional removal of the phenol proper, the cresols could then be recovered in pure form with one operation.

The production of purified cresols is, therefore, a logical opening for American enterprise, as well as American resources, for here, as in Europe, are immense supplies of coal tar on which to draw for crude materials.

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### BENZYL BENZOATE.\*

As the drug has come into fairly extensive use, some notes on its pharmacy, chemistry, and general properties may be of service.

Benzyl benzoate,  $C_6H_5COO.C_6H_5CH_2$ , is the benzyl alcohol ester of benzoic acid. It occurs naturally in several of the balsamic resins, such as balsam of Peru and in balsam of tolu. Possibly the antispasmodic action of these drugs is due in some measure to its presence. It is contained in the volatile oils of many fragrant flowers, such as hyacinth, jasmin, orange, etc. It may be obtained by the fractional distillation of the oily portion of balsam of Peru; it is made synthetically in several ways. On a manufacturing scale it may be prepared either by treatment of benzyl chloride and benzoic acid with phosphorus oxychloride, or by treatment of benzyl chloride and sodium benzoate with soda ash.

It is a colorless oily liquid, odorless or with a faint aromatic odor, and having a sharp burning taste. It is insoluble in water or glycerin, but is miscible in all proportions with alcohol, chloroform, or ether. When ignited it burns with a smoky flame. Sp. Gr. 1.09 to 1.13 at  $15^{\circ} C$ . It is neutral to litmus. Alcoholic solution of KOH saponifies it readily. This solution when neutralized gives with ferric chloride a flesh-colored precipitate, and upon acidulation a white, crystalline precipitate of benzoic acid separates. This may be extracted with ether and identified by means of the usual tests for benzoic acid. Benzyl benzoate for medicinal purposes should be free from chlorine and should contain not less than 95 per cent. of pure benzyl benzoate. The residue from ignition of 10 Cc. should weigh not more than 0.1 Mgm., that is, practically *nil*. The volumetric test given by the American Medical Association is as follows: To about 2 Gms. benzyl

\*From *The Prescriber*, March, 1920.

benzoate, accurately weighed, add 25 Cc. half-normal alcoholic KOH and heat the mixture to incipient boiling under a reflux condenser for one hour. To the cooled solution add phenolphthalein and titrate the excess KOH with half-normal HCl. Each gram of benzyl benzoate requires for saponification not less than 8.9 or more than 9.4 Cc. of half-normal KOH.

The dose of benzyl benzoate is 0.3 to 0.5 mil. (5 to 7 minims). It may be given in 20 per cent. alcoholic solution (dose, 20 to 30 drops). A proprietary emulsion contains benzyl benzoate 20 Gm. in alcohol 78 Gm. to which 2 Gm. of castile soap is added as an emulsifying agent. Gum acacia may also be used as emulsifier.

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### A PROBABLE NEW SOURCE OF GINGER.\*

In times like the present, when every bit of information affecting the increased production of vegetable products, whether for food, medicine, or manufacture, is especially valuable, the following extracts from an article on "Wild Ginger" in a recent number of the *Agricultural News* cannot fail to be of interest. It may be stated that the *Agricultural News* is one of the official publications of the Imperial Department of Agriculture for the West Indies. It is pointed out that the true ginger plant (*Zingiber officinale*) is not known in a wild state, but that it is doubtless a native of tropical Asia, where it has been cultivated and from where the rhizomes have been exported from very remote times. From Asia it was introduced into the West Indies, and has spread now throughout the warmer parts of both hemispheres. The name "ginger" is derived through the Greek from the ancient Sanscrit. It was known as a spice to the early Greeks and Romans. During the Middle Ages it is frequently mentioned in European lists of articles derived from the Far East. In an interesting account of a journey down the Magdalena River and through the Peninsula of Goajira undertaken at the request of the Minister of Agriculture and Commerce of the Republic of Columbia for the purpose of studying the agricultural conditions and possibilities of the region, Mr. M. T. Dawe, F.L.S., Agricultural Adviser to the Government of Columbia, makes the interesting statement that he found ginger growing wild over extensive areas on the

\* From *The Chemist and Druggist*, Feb. 7, 1920.

lower hills of the Sierra Nevada range. He thinks, therefore, that the theory that ginger was originally a native of tropical South-East Asia must be abandoned and Columbia be considered its original habitat. This, however, would be open to question, for it is quite certain that ginger was introduced by the Portuguese into Brazil as early as the middle of the sixteenth century, and it is probable that the ginger now found growing wild in Colombia is really only the descendant of plants escaped from cultivation which have become thoroughly naturalized. Mr. Dawe goes on to remark that this discovery is of commercial importance, owing to the fact that there are extensive wild sources of a valuable product which can be immediately exploited and a new local industry established in the collection and preparation of the roots. Apart from the question of the exploitation of the wild product, there raises the possibility of its cultivation and the initiation of a new plantation industry for that part of Colombia. Ginger is well known to be fastidious as to its soil requirements, and the fact that it is found growing wild is a proof that not only the climate but the soil is suitable to it. The rhizomes of the wild plant, however, are not nearly so large as those of the cultivated ginger. Mr. Dawe adds a word of warning to intending exporters of ginger, whether wild or cultivated, to the effect that whatever method of curing and drying be employed, the rhizomes must be thoroughly dried and bleached before shipment. The cultivation of ginger in the Kandy district of Ceylon is also the subject of a note in the *Tropical Agriculturist*, in the course of which it is stated that the area under ginger is extending in the island. In the Kandy district during 1917-18 eighty acres, yielding 480,000 lbs. of green ginger, equal to about 850 cwt. dry ginger, was obtained, and particulars are given as to how this was raised, the seed being obtained from India. Ceylon could easily produce a large quantity of ginger, but the chief obstacle is that the villagers are ignorant of the method of curing it for the market. Locally there is always quite a good demand for green ginger, which sells at 12 to 15 cents, and even 20 cents to 25 cents per lb., so that there are no exports. It would be worth consideration whether a profitable business could not be started in curing ginger for the market, as a well-cultivated, good crop may yield up to 15,000 lbs. to the acre. At the present time most of the ginger imported into London is produced within the British Empire, but there is no reason why Ceylon should not make it a paying minor product.

## PRODUCTION OF GLYCERIN FROM SUGAR.\*

(Prepared by the Research Division, Bureau of Foreign and Domestic Commerce.)

At the beginning of the war Germany was "swimming in sugar," to use an expression of the *Frankfurter Zeitung* (May 22, 1915). Production had been greater than ever; large quantities left from the previous campaigns were still available; exportation had stopped. One of the 10 "war commandments," proclaimed on bills posted in all railway stations, advised people: "Use plenty of sugar with your meals; sugar is an excellent food." Certain measures of the Government, however, soon made it impossible for the people to follow that advice, and sugar became scarce in the market, although it was known that stocks were plentiful, for the production of the 1913-14 campaign had yielded 2,715,870 metric tons of sugar. Germany had been the leading sugar-producing country of Europe, and yet the people suffered from scarcity of sugar during the war and were compelled to use honey and saccharin as substitutes. It was supposed that owing to the shortage of fats the Government was trying to conserve the stocks of sugar. It now appears that large quantities of sugar that had been withdrawn from human consumption were used in the manufacture of glycerin for war purposes. The process of production is described by Dr. W. Constein and Dr. K. Ludecke in *Die Naturwissenschaften* (1909, p. 403).

*Process of Production.*—The consumption of glycerin in the manufacture of cosmetics and for other purposes, chiefly in the manufacture of explosives, increased enormously during the war, while the supply of the raw materials—fats—was constantly diminishing. It was therefore necessary to seek other sources, and sugar was selected, as its chemical structure is somewhat similar to that of glycerin. The transformation of sugar into glycerin was accomplished by the biochemical method. It has been known for a long time that in the ordinary fermentation of sugar with yeast small quantities of glycerin would be produced, amounting to about 3 per cent. of the sugar. By adding alkalies to the liquid in fermentation the production of glycerin was increased. It was found that almost any salt with an alkaline reaction could be used for that purpose. Experiments were made with acetate, bicarbonate, and dibasic phosphate of sodium and with carbonate of ammonia.

\* *Commerce Reports*, Feb. 3, 1920.

The yield of glycerin was increased to 12.7 per cent. but the alkaline mash was found to be an excellent breeding place for all kinds of acid-forming bacteria which would pollute the glycerin. This fault was remedied by the use of sodium sulphite which acts as a poison to the bacteria of lactic acid and others but does not, even in large quantities, affect the yeast cells (*Saccharomyces*). When sodium sulphite was employed as an antiseptic the yield of glycerin was increased proportionately to as much as 23 to 36.7 per cent. of the sugar.

The ordinary fermentation produces not only alcohol, carbonic acid, and glycerin, but also small quantities of acetaldehyde. When the sulphite is added in increasing quantities the yield of acetaldehyde and glycerin increases, while that of alcohol and carbonic acid decreases. The acetaldehyde was used largely for war purposes. The production of glycerin from sugar had a great practical value in war time, according to German writers. The manufacturing process, patented in 1915, was exploited on a large scale, and the production of glycerin exceeded 2,200,000 pounds a month. The invention also possesses an unusual theoretical interest as it shows how the transformation of materials by bacteria can be influenced by the addition of chemicals. In the words of a German writer (Prometheus, Nov. 1, 1919), "the biochemical processes open up new prospects for the future and seem to be destined to provide many substitutes to a people robbed of all raw materials."

Attempts made during the war in Austria-Hungary to produce glycerin from sugar do not seem to have met the success claimed for similar attempts in Germany. Complaint was made by the Bohemian journals of Prague that carloads of sugar had been wasted in recovering negligible quantities of glycerin, and doubts were expressed whether such waste of food could be justified even by the exigencies of war.

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## ANNUAL MEETING OF THE PHILADELPHIA COLLEGE OF PHARMACY.

The Annual Meeting of the Philadelphia College of Pharmacy was held at the College March 29, 1920, at 3.00 P.M., the President. Howard B. French, presiding. Thirty-four members were present.

President French read his annual address. The address gave in detail the condition of the buildings, the work of the various de-

partments, the classification of the students as to numbers in the different courses of instruction and many items of interest in connection with the College work.

The following abstract from this interesting address covers special recommendations relating to the Centenary of the Founding of the College:

"Your President regrets that he cannot report success in obtaining a site upon the Parkway for your new buildings. The matter, however, is in the hands of the Park Commission and he hopes in the near future to be able to submit to them for their consideration, a sketch of the elevation for your buildings. He feels confident that provisions will be made in the very near future for the proper location of your College upon or adjacent to the Parkway.

"In about a year we shall be called upon to celebrate our 100th anniversary and it has been suggested at a conference of some of your members that an anniversary volume be issued shortly after the memorial exercises, which in the opinion of your President, should be in June, 1921, at the time of the annual commencement. In addition to the report of the exercises, it is thought that a complete historical account should be given concerning the College and its development—including photographs (so far as can be obtained) and sketches of those members who have taken an active part in the conduct of your institution from its origin in 1821 to the Centenary. A complete list of the graduates of the College, with short biographical sketches of all that it is possible to obtain should be published in this volume.

"This work, which will prove no small task, should be placed in charge of a proper Committee, which, with your sanction, should be appointed by your executive. The Committee should in his judgment be a combined College, Faculty and Alumni Committee.

"Your Board of Trustees have already placed themselves on record as favoring a certain type of building and placed the preparation of plans for the same in the hands of a committee.

"Efforts should also be made to use every means to secure funds for the development, maintenance and endowment of the institution. No better work could be placed in the hands of an active Alumni Committee, which should work in full accord with the Committee appointed by the authorization of your body.

"It is the wish of your Executive that at this meeting you authorize him to appoint such committees as in his judgment and

with the approval of your Board of Trustees, would prove efficient in carrying out the suggestions made above. He particularly asks that you authorize him to appoint an 'Executive Secretary of the Centenary Plan.' Such a secretary should be a person of energy and enthusiasm to whom could be entrusted the task of formulating the details of the comprehensive plan under the supervision and guidance of the existing Committee of the Board of Trustees."

Joseph W. England offered the following:

"*Resolved*, That a General Committee on the One-Hundredth Anniversary of the College, representing every pharmaceutical interest and every section of the country, and sub-committees of this General Committee, be appointed by the President; the chairmen of the various sub-committees to constitute an Executive Committee," which was, on motion, adopted.

Robert P. Fischelis offered the following resolutions:

"*Resolved*, That it is the sense of this meeting that the General Committee on Centenary, to be appointed in accordance with the resolution offered by Mr. England, shall consist of one hundred and include representatives of the Alumni, Faculty, Trustees and Members of the College, and shall be headed by the President of the College.

"*Resolved, further*, That ten members of this General Committee, residing in Philadelphia or within easy access of the City, be designated at once by the President as a 'Sub-Committee on Organization,' to work out a plan covering the various activities to be entered into and the manner in which they are to be handled in connection with the Centennial Celebration, and submit the same for approval at a special meeting of the College to be called for that purpose within one month."

This was amended "that the Executive Secretary be selected at once and be added to the Committee of Ten."

The resolutions were fully discussed by many of the members and unanimously adopted, and April 26, 1920, was fixed as the time for the special meeting of the College.

Report of the Committee on Publication was read by Prof. Charles H. LaWall and on motion the report was received and the recommendation of the Committee that the College appropriate the usual amount for the use of the AMERICAN JOURNAL OF PHARMACY for the year 1920 was adopted.

The following is a brief statement of the progress of the JOURNAL since 1917:

Increase in mailing list.....	132 per cent.
Increase in total revenue.....	99 " "
Increase in publication expenses....	82 " "

The advanced cost of most everything has materially affected the printing trade, but it is hoped that the cost of publication has about reached its height.

Prof. LaWall stated that the estate of the late Prof. Henry Trimble had sent to the JOURNAL a complete set of the AMERICAN JOURNAL OF PHARMACY. On motion, the thanks of the College were tendered to Mrs. Trimble for the valuable donation.

The Editor, Mr. George M. Beringer, reported that Volume 91 of the JOURNAL had been completed, and the monthly numbers are being issued as promptly as the demoralized condition of the printing trade permitted. Volume 91 contained a variety of original contributions, editorials, abstracts, and reprints from current literature, the purpose being to recognize the needs and desires of each branch of pharmacy and the drug trade interests. The primary duty of journalism, in whatsoever field engaged, is to make the publication sound, representative, progressive and beneficial to the interests it professes to serve. In order to fulfil its obligations to pharmacy, the scope of the AMERICAN JOURNAL OF PHARMACY had to be broadened and its circle of influence widened. The JOURNAL must continue to be the torch-bearer that will illumine the path of advances and record the progress of pharmacy and the allied sciences. The JOURNAL is developing a policy and taking an active interest in all matters pharmaceutic and by so doing its usefulness to pharmacy is receiving more recognition and its influence is growing apace. In a marked way this is shown in the growth of the list of subscribers. The earnest and hearty coöperation of the Committee on Publication, business management and contributors is gratefully acknowledged and to these the thanks of the College must be accorded for making possible the continued success and prosperity of the JOURNAL.

Mr. George M. Beringer reported the death recently of M. Eugène Collin, of France, an honorary member of the College.

Committee on Necrology reported that but one active member of the College had died during the year—Mr. C. Carroll Meyer.



An appropriate obituary has been prepared by Prof. Frank X. Moerk and published.

Prof. Cook, for the Committee on Nominations, reported that the list of nominations for officers had been printed and sent to all the members.

Prof. F. P. Stroup, who had been acting as librarian *ad interim*, reported verbally that the library had been used more than in any similar length of time for many years.

President French read a communication from Prof. Charles H. LaWall in which he suggested that the Pennsylvania Pharmaceutical Association be invited to hold their meeting in 1921 in Philadelphia at the time the College was holding its Centenary celebration. He believed hundreds of the Alumni would come to the city then, attracted by the double event. In the discussion that followed the reading, it was suggested that other organizations should also be invited to hold their meetings about that time. The suggestion was favorably received, when, on motion, it was voted to tender to the Pennsylvania Pharmaceutical Association the use of the College to hold their meeting in 1921.

President French read the following communication:

Camden, N. J., March 24, 1920.

"MR. HOWARD B. FRENCH, *President*,  
Philadelphia College of Pharmacy,  
Philadelphia, Pa.

DEAR SIR:

The New Jersey Pharmaceutical Association have had engrossed and framed resolutions upon the death of Prof. Remington. They desire to present these to the College as a token of their esteem for the late professor.

I understand that the next quarterly meeting of the College will be on Monday afternoon, March 29. If it is agreeable to you I will be glad to present this memorial at that time on behalf of the New Jersey Association.

Yours truly,

(Signed) GEORGE M. BERINGER, JR."

Mr. Beringer, Jr., being present, was invited to the floor, and in very appropriate remarks, presented the resolutions to the College. On motion, the sincere thanks of the College were tendered the New Jersey Association for the gift.

Prof. Heber W. Youngken, Curator, reported that one of the conditions growing out of the prohibition laws was the necessity of having a bond executed because of the many alcoholic preparations in the College. The alcohol question is now settled and we are getting our quota of alcohol for scientific purposes.

Mrs. F. M. Apple presented a crude drug specimen case.

Prof. LaWall had secured a section of wood water pipe used in the city about 1820.

The Martindale herbarium was being cleaned. The herbariums are being numbered to correspond with the Martindale herbarium. Some changes have been made in the classification and other changes are in prospect.

As the result of the ballot taken, the following officers were elected:

President, Howard B. French.

First Vice-President, R. V. Mattison, M.D.

Second Vice-President, Joseph L. Lemberger.

Treasurer, Aubrey H. Weightman.

Corresponding Secretary, C. A. Weidemann, M.D.

Curator, Heber W. Youngken.

Editor, George M. Beringer.

Librarian, F. P. Stroup.

Trustees—C. Stanley French, George B. Evans, Ambrose Hunsberger, Warren H. Poley.

Committee on Pharmaceutical Meetings—C. B. Lowe, M.D., George M. Beringer, Charles H. LaWall, John K. Thum, Heber W. Youngken.

Publication Committee—Joseph W. England, Charles H. LaWall, George M. Beringer, John K. Thum, J. W. Sturmer, R. P. Fischelis, E. F. Cook.

The President made the following appointments:

Committee on By-Laws—George M. Beringer, Joseph W. England, C. A. Weidemann, M.D.

Delegates to the American Pharmaceutical Association—Charles H. LaWall, J. W. Sturmer, F. P. Stroup, E. Fullerton Cook, C. B. Lowe, F. X. Moerk, H. W. Youngken, John K. Thum.

Delegates to Pennsylvania Pharmaceutical Association—Charles H. LaWall, J. W. Sturmer, C. B. Lowe, E. Fullerton Cook, F. X. Moerk, O. W. Osterlund.

Delegates to the New Jersey Pharmaceutical Association—

George M. Beringer, Charles H. LaWall, J. W. Sturmer, C. B. Lowe, H. W. Youngken.

Delegates to the Delaware Pharmaceutical Association—A. W. Miller, H. J. Watson, S. Loraine Foster.

Delegates to the Conference of Pharmaceutical Faculties—Charles H. LaWall, J. W. Sturmer, F. P. Stroup, H. W. Youngken.

On motion of R. P. Fischelis, it was voted that the College send a congratulatory message to the New Jersey Pharmaceutical Association on the occasion of the celebration of its Fiftieth Anniversary this coming summer.

Dr. Wm. Duffield Robinson stated he had conversations with a number of physicians who were also graduates of the Philadelphia College of Pharmacy, and who were favorably impressed with the idea of the Centenary celebration, and he suggested the appointment of a Committee to consider organizing the physician-pharmacists into an alumni association for the purpose of aiding the College and contributing to the success of the Centenary celebration. After some discussion, Dr. Robinson moved that the President appoint a committee to consider such an organization. Seconded and so ordered.

A symposium on the Centenary celebration followed. Prof. E. F. Cook was the first speaker. He was very enthusiastic and optimistic over the project. He thought the Alumni Association would be very active. Groups in every organization could be utilized. He wanted to see the College heartily sustained as a leader in the science of pharmacy, as well as in practical work; the advanced courses recently introduced and the extension of research work were dominant factors in maintaining the standing of the College.

R. P. Fischelis mentioned the recent celebration of the 100th anniversary of Colgate University. They had an enthusiastic Alumni Association and one of great activity. Fifteen hundred of its three thousand graduates were present and had worked hard for the success of the celebration. It was an object lesson for us. Publicity work was needed to attract students, and the student co-operation was desirable, and that of many others, especially the help of the large manufacturing houses of the country, a number of whom had in their organizations graduates of the P. C. P.

Dr. P. S. Stout was in favor of the suggestion of Dr. Robinson. It would be one element of success in the Centenary campaign.

Dr. Stewart also approved of the suggestion of Dr. Robinson. It would give us a good deal of backing from our medical graduates.

Mr. McNeary thought it desirable for the officers and trustees of the College to enlist the coöperation of and secure contributions from those who are among our graduates who have become millionaires because of the influence on their lives and their great success in life their connection with the College has had.

Mr. George M. Beringer was glad we had gotten down to a definite plan of work. We had talked much previously, but from to-day we are going to get down to hard work. This celebration was not a local affair, it was a national, yes, even an international event. Let us make a big function of it.

Prof. LaWall suggested to get the American Pharmaceutical Association to meet here next year. This was very favorably received, and, on motion, it was

"Resolved to formally extend an invitation to the American Pharmaceutical Association to meet in Philadelphia in 1921 and join with us in celebrating the Centenary of the College."

Mr. Beringer, Jr., said this would practically be a celebration of the centenary of pharmaceutical education in this country, and he thought that the beginning of pharmacy in Philadelphia had not been as well understood as it should be.

Mr. French suggested that the New Jersey Pharmaceutical Association should also meet in Philadelphia in 1921.

Mr. Beringer had often hoped for a joint meeting with the Pennsylvania Pharmaceutical Association—he thought it would be appropriate to ask the New Jersey Association to meet about the time of the Centenary celebration and hold at least one of their meetings in the College. The suggestion was favorably received, and, on motion, was adopted.

Mr. R. T. Blackwood proposed extending an invitation to the National Association of Retail Druggists to meet in Philadelphia in 1921.

Prof. LaWall proposed inviting the Conference of Pharmaceutical Faculties, and the National Association of Boards of Pharmacy.

A member proposed inviting the Philadelphia Association of Retail Druggists to actively participate in the centennial events.

All of these propositions were adopted.

Prof. LaWall moved that a Publicity Committee be appointed. Seconded, approved and so ordered.

In conclusion, Mr. Cliffe moved that we take cognizance of all pharmaceutical organizations. Approved.

C. A. WEIDEMANN, M.D.,  
*Recording Secretary.*

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## NEWS ITEMS AND PERSONAL NOTES.

### DRUG TRADE BOARD OF PUBLIC INFORMATION ORGANIZED.

Representatives from eight national pharmaceutical associations met at the Chemists' Club, New York City, March 8, 1920 and organized the Drug Trade Board of Public Information. The object of this organization is to supply the public press with information regarding the various branches of pharmacy and secure for the profession that recognition to which it is entitled at the hands of the public and which it is not now receiving. The meeting was the outgrowth of the plan submitted by the Committee on Federation of the American Pharmaceutical Association at the meeting of the latter last August. The associations represented and their representatives are as follows:

National Wholesale Druggists' Association, C. H. Waterbury and F. E. Holliday, Mr. Waterbury being the permanent representative.

National Asso. Boards of Phar., Jacob Diner.

Am. Conference Phar. Faculties, Edwin S. Newcomb.

Am. Asso. Pharmaceutical Chemists, H. Noonan.

Proprietary Asso. of America, E. F. Kemp.

Nat'l Asso. Retail Druggists, Samuel C. Henry.

American Pharmaceutical Asso., Robert P. Fischelis.

Dr. H. V. Army, chairman of the sub-committee on organization of the American Pharmaceutical Association, called the meeting and presided until the committee was able to organize. A temporary organization was formed with C. H. Waterbury, chairman, and R. P. Fischelis, secretary and treasurer. This temporary organization will function until May 10, when another meeting will be held in Washington at which the constitution and by-laws will be adopted and plans for active work will be presented. Members of the Board are now at work in planning for future activities. Business is being

carried on by correspondence and it is felt that when the permanent organization is formed in May, American pharmacy will at last have an organization as representative as the Drug Trade Conference, which will act as the mouth-piece of pharmacy in relation to the general public.

## THE PENNSYLVANIA BOARD OF PHARMACY.

### *Notice of Examinations.*

Examinations for applicants desiring registration as Pharmacists, will be conducted in the Philadelphia College of Pharmacy, 145 North Tenth Street, Philadelphia, and the Pittsburgh College of Pharmacy, corner Pride and Bluff Streets, Pittsburgh, on Friday and Saturday, June 4 and 5, 1920.

### TIME AND PLACE.

#### PHARMACIST EXAMINATION.

*Practical Pharmacy*—Friday, June 4, 1920. Class No. 1, at 9 o'clock A.M.; Class No. 2, at 11 o'clock A.M.

*Materia Medica*—Friday afternoon, June 4, 1920, 2.30 to 6 o'clock.

*Chemistry*—Saturday morning, June 5, 1920, 9 to 12 o'clock.

*Pharmacy*—Saturday afternoon, June 5, 1920, 2 to 6 o'clock.

#### ASSISTANT PHARMACIST EXAMINATION.

*Pharmaceutical Arithmetic, Posology, Toxicology*—Saturday morning, June 7, 1920, 9.30 to 12 o'clock.

*Pharmacy, Materia Medica*—Saturday afternoon, June 5, 1920, 1.30 to 6 o'clock.

*Assistant Pharmacist Examination*—At the Pittsburgh College of Pharmacy, corner Pride and Bluff Streets, Pittsburgh, Pa., and the Philadelphia College of Pharmacy, 145 North Tenth Street, Philadelphia, Pa., on Saturday, June 5, 1920, 9.30 to 6 o'clock.

L. L. WALTON, *Secretary*,

P. O. Box No. 265, Williamsport, Pa.

## LEHN & FINK, INC., MOVE TO NEW HOMES.

Forty-five years ago, Lehn & Fink, Inc., was doing business in one floor, cellar and sub-cellar of a small building at 160 William Street, New York City. The firm soon had to seek larger quarters,

which were found at 128 William Street. This shortly became inadequate and the well-known Lehn & Fink Building at 120 William Street was erected. Laboratories and manufacturing plants were built in Brooklyn, N. Y.

Increased business had again overtaken Lehn & Fink, Inc. A site of 20 acres of land, located on two trunk line railroads at Bloomfield, N. J., with ideal motor-trucking facilities to New York and with convenient trolleys for Newark and other sections of New Jersey, was purchased when it became evident greatly augmented manufacturing facilities would soon be necessary.

Despite uncertain weather and building conditions, new, modern manufacturing plants and laboratories were put up on this site during the winter and early spring. All departments of the plant are now in full operation directed by experts. The whole organization at Bloomfield has been planned to facilitate a maximum production and many new time and labor saving devices have been installed.

Research and testing laboratories occupy a prominent place in the new buildings, and rigid inspection is maintained to insure the quality.

The buildings contain every comfort for employees—abundant sunshine on every floor, ample wash rooms, lunch rooms and thorough ventilation.

Power is supplied from dynamos driven by oil-burning boilers. The water comes from newly driven artesian wells. A machine shop and box factory complete the equipment designed to make these laboratories and manufacturing plants a self-sustaining unit.

#### A NEW MODERN BUILDING IN NEW YORK.

During the summer, Lehn & Fink's executive offices and stock rooms will be moved to the 170,000 square feet of floor space in a new steel and stone building at Greenwich, Morton and Barrow Streets, New York City.

#### P. C. P. STUDENTS VISIT THE H. K. MULFORD CO. LABORATORIES.

The Philadelphia College of Pharmacy class of 1920 were the guests of the H. K. Mulford Company, on the afternoon of March 18, and visited the Biological Laboratories at Glenolden, Delaware County, Pennsylvania.

Special train service of three coaches was provided, which were well filled—there being one hundred and seventy-five in the party. Souvenir programs were prepared for the occasion, and as the weather was ideal, the trip was a most enjoyable one. The expressions of appreciation were universal.

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## CURRENT LITERATURE.

### SCIENTIFIC AND TECHNICAL ABSTRACTS.

DETECTION OF NICOTINE.—O. Tunmann (*Apoth. Zeit.*, 33, 485, 1918; through *Chem. Zeit. Rep.*, 43, 193, 1919).—A drop of the alkaloid solution is brought into contact with a small quantity of *p*-dimethylaminobenzaldehyde dissolved in a drop of concentrated hydrochloric acid. Nicotine yields a red coloration which soon changes to violet-red; the reaction may be obtained with as little as 0.2 Mgm. of nicotine. Pyridine, coniine, and the common alkaloids do not interfere with the test. With a cold saturated picric acid solution containing 10 per cent. of concentrated hydrochloric acid, 0.01 Mgm. of nicotine yields a distinct precipitate, while 0.003 to 0.005 Mgm. gives microscopic crystals (these appear in about two minutes); pure pyridine also gives crystals with this test, but no amorphous precipitate. (From *The Analyst*, December, 1919.)

DETECTION OF HYDROGEN CHLORIDE IN CHLOROFORM.—D. Vorlander (*Ber. Deut. Pharm. Ges.*, 28, 337, 1918; through *Chem. Zeit. Rep.*, 43, 193, 1919).—Ten Cc. of the chloroform are treated with a very small quantity (about 0.01 Mgm.) of powdered *p*-dimethylaminoazobenzene, if hydrogen chloride is present a violet-red coloration is obtained. In the absence of hydrogen chloride the chloroform is colored yellow. An excess of the reagent may mask the coloration given by very small traces of hydrogen chloride. The violet-red coloration is destroyed by free chlorine. (From *The Analyst*, December, 1919.)

ANALYSIS OF SACCHARIN.—O. Beyer (*Chem. Zeit.*, 43, 537-538, 1919).—As the result of an examination of methods which have been proposed for the estimation of saccharin, the author finds that only



two methods are useful: namely, Richmond and Hill's method (cf. *Analyst*, 43, 353, 1918), and the *Reichsgesundheitsamt* method. According to the latter method 0.5 to 0.7 Gm. of the sample is boiled for two hours under a reflux condenser with 20 Cc. of 20 per cent. sulphuric acid, the solution then cooled, diluted, rendered alkaline with sodium hydroxide, and distilled, the ammonia being collected and titrated in the usual way. When the melting-point of a sample of commercial saccharin falls below  $220^{\circ}$  C., it is advisable to estimate the amount of *p*-sulphaminobenzoic acid present. For this purpose, 1 Gm. of the sample is heated for two hours under a reflux condenser with 10 Cc. of hydrochloric acid (sp. gr. 1.124) and 10 Cc. of water; the solution (filtered if necessary) is evaporated to dryness on a steam-bath, the residue dissolved in 10 Cc. of hot water and the solution kept for at least twelve hours at a temperature below  $10^{\circ}$  C. The para acid separates out as crystals, which are collected, washed with a small quantity of cold water, dried at  $100^{\circ}$  C., and weighed. (From *The Analyst*, December, 1919.)

ESSENTIAL OIL FROM *Juniperus procera* GROWN AT NAIROBI.—A. F. Macculloch (*J. Soc. Chem. Ind.*, 38, 364-T, 1919).—The oil obtained by steam distillation of fine shavings of the wood of *Juniperus procera* grown at Nairobi, British East Africa, had the following characters: Sp. gr. 0.987 at  $15.5^{\circ}$  C.  $[a]_{D_{20}} = -16^{\circ}$ ,  $[n]_{D_{20}} = 1.480$ . The oil was miscible in all proportions with alcohol of 90 per cent. and over, soluble (1 : 60) in 70 per cent. alcohol. The amount of cedrol formed depended on the interval between the disintegration and distillation of the wood. After exposure of the wood for some weeks to a hot sun the distilled oil solidified to a mass of crystals. The oil obtained by distilling wood which had not been exposed to the sun after disintegration contained 38 per cent. of cedrol (m. p.,  $75.5^{\circ}$  C.). (From *The Analyst*, December, 1919.)

OIL FROM SUMAC (*Rhus Glabra*).—H. W. Brubaker (*J. Ind. Eng. Chem.*, 11, 950, 1919).—The seeds separated from sumac berries yielded on extraction with ether 11.71 per cent. of fatty oil, the average characters of which were as follows: Sp. gr. at  $15^{\circ}$  C., 0.92577;  $[n]_{D_{20}} = 1.4710$ ; acid value, 0.9; acetyl value, 9.235; saponification value, 192.6; iodine value, 126.76; soluble fatty acids, 0.766; insoluble fatty acids, 93.54 per cent. The characters of the insoluble fatty acids were: M. p.,  $17^{\circ}$  C.; solidifying pt.,  $6^{\circ}$  C.;

$[n]_D$ , 1.470; iodine value, 121.8. The oil is quite viscid at ordinary temperature, and has a mild odor; it possesses moderate drying properties, and compares favorably with other vegetable oils, such as cottonseed oil. It is applicable as an edible oil or as a material for soap making, or as a semi-drying oil for paints. It is estimated that 6 million lbs. of oil could be obtained annually from sumac seed in the State of Kansas. (From *The Analyst*, December, 1919.)

A NEW ESSENTIAL OIL.—Challinor, Cheel and Penfold describe in *J. Proc. Roy. Soc., N. S. W.* (52: 175, 1918), the essential oil obtained from the entire plant of a new species of *Leptospermum* (*L. citratum*). It is of a pale amber color and pleasant lemon-oil odor, sp. gr. at  $\frac{15^\circ}{15^\circ}$  C., 0.8841; Opt. rotat. at  $18.6^\circ$  C.,  $a_D + 3.6$ , refract. ind. at  $20^\circ$  C.;  $n_D$  1.4730. It contains 90 per cent. of the aldehydes citronellol and citral in nearly equal proportions, and is soluble in two volumes of 70 per cent. alcohol (by weight). The identification of the two aldehydes was made by the approved methods. The non-aldehydic portion of the oil is still under examination, as the amount available is small. A small proportion of a phenolic substance seems to be present as a crystalline benzoate is produced by the action of benzoyl chloride. Color reactions with bromine and with hydrochloric acid indicate the presence of a small amount of aromadendrene. The data show that the oil is distinctive in character and differs from that of any other species of *Leptospermum* so far recorded.

H. L.

BOTULISM.—The experiments reported on by Dickson and his associates were undertaken to determine the thermal death point of *B. botulinus* and its spores under various conditions. They found that the spores of *B. botulinus*, when mixed with animal and vegetable protein, are much more resistant to heat than has been believed. The acidification of the culture medium by the addition of 5 per cent. lemon juice does not prevent the growth of *B. botulinus* or the formation of its toxin, but the thermal death point of spores of *B. botulinus* is markedly lowered when they are heated in an acid medium of similar concentration. The addition of cane sugar to beef broth in concentration up to 64 per cent. does not prevent the growth of *B. botulinus* or the formation of its toxin, although it does inhibit both to a certain extent. Certain fruits which have been

canned in sugar form suitable mediums for the growth of *B. botulinus* and the development of its toxin. Peaches, apricots and pears were tested. Certain of the methods of canning are inefficient if the raw material happens to be contaminated with spores of *B. botulinus*. This is true of commercial canners' processes as well as of the home canning processes. (*Arch. Intern. Med.*, Chicago; through *J. Am. Med. Assoc.*, January 10, 1920.)

MODIFICATION OF BENZIDINE TEST FOR OCCULT BLOOD.—Gregersen has recently found that a frequent cause of failure in the application of the benzidine test is that too strong solutions of the reagent are used. Following Grundmann's idea, he reached the conclusion that many of the positive reactions in normal persons on a meatless diet may be explained by the fact that mineral traces of blood were mixed with the feces, which, because of the excessive sensitiveness of the reagent, produced positive reactions. Boas accepts the idea that the use of highly concentrated benzidine solution doses lead to false diagnosis, and on that account approves, after careful trials, Gregersen's modification of the test. Gregersen uses a 0.5 per cent. benzidine solution, and instead of the easily decomposable hydrogen dioxide he employs barium dioxide, which is much more stable. Gregersen's method is described in detail, and Boas offers what he considers a further slight improvement. Boas admits, however, that in using the weaker solution very slight hemorrhages, though worthy of note, might go undiscovered. (*Berliner klinische Woch.*; from *Jour. Amer. Med. Assoc.*, January 24, 1920.)

DETERMINATION OF FILICIC ACID.—Perrin (*Repertoire de Pharmacie*, No. 3, 1919) states that it is essential to determine the amount of filicic acid present in extract of male fern, as many an extract may have the required content of filicin, without containing a trace of filicic acid, the essentially active constituent. He employs the following method: to the crude filicin, in the weighed flask, obtained according to the directions given in the B. P., add 2 Cc. of amylic alcohol, allow the mixture to stand for twenty-four hours, well corked, shaking occasionally. Thereupon, drop by drop, 20 Cc. of pure methyl alcohol are added; the first drops produce a precipitate which redissolves; when the precipitate does not redissolve the remainder of the methyl alcohol may be added at once. Shake, let the mixture stand for twenty-four hours in a cool place; filter, wash

out the flask, then the filter, twice with 5 Cc. of methyl alcohol; allow the filter to dry; then place the filter and the flask in a cold oven and gently heat to  $100^{\circ}$ , allow them to remain at  $100^{\circ}$  for one hour; then weigh. The amount of filicic acid contained in the flask, *plus* the filicic acid on the filter multiplied by 25, gives the content of filicic acid in 100 grams of the extract; the amount should be from 3.5 to 9 per cent., according to the date of harvesting the male fern; while the content of filicin scarcely varies, the amount of filicic acid present is higher in autumn than in spring. (From *The Chemist and Druggist*, January 10, 1920.)

FRAUDULENT COCAINE.—Samples of a substance carefully packed in tins and labelled cocaine hydrochloride and sold on the German market have been found to consist of magnesium sulphate in unusually minute crystals which seem to have been especially prepared to perpetrate the fraud. (*The Pharm. Jour. and Pharmacist*, September 27, 1919.)  
J. F. C.

POISONING CROWS WITH STRYCHNINE.—Crows have become a serious menace to the almond crop in Klickitat County, Wash. Green almonds impregnated with strychnine (strychnine sulphate?) have been found very satisfactory in exterminating the birds. (*Weekly News Letter*, U. S. Dept. Agric., January 28, 1920.)  
J. F. C.

SIMPLIFIED METHOD FOR DETECTION AND ESTIMATION OF DISTRIBUTION OF MORPHINE.—The presence of morphine in food, or in tissues and body fluids, has been determined by Morgulis and Levine by heating with 2 per cent. tartaric acid (if solid, the material should first be ground or finely minced) to convert all morphine into the soluble tartrate. The mixture is rapidly cooled, preferably on ice, to solidify the fatty material. The solid residue is removed by straining through cheese-cloth, and is washed until the washings are no longer acid to litmus. The liquid, after being filtered through paper, is evaporated to a pasty consistency. The tartrate is then decomposed by the addition of an excess of sodium bicarbonate which sets the alkaloid free. The evaporation is then continued to complete dryness, and the mass is powdered and extracted with chloroform to remove the free morphine. The volume of the chloroform extract is noted, and the smallest quantity of the

extract is found which, on evaporation (in a porcelain crucible over the water bath), leaves a residue which yields a definite morphine test. In this way the relative amount of morphine in several extracts can be determined. Besides knowing the limit of sensitivity of the reaction an approximate estimate of the amount of morphine in the original sample is possible. Inasmuch as the authors found that morphine, whether given subcutaneously or by mouth, is widely distributed throughout the animal body, finding its way into almost every tissue, they state, that it is not advisable to limit the toxicologic examination for morphine to the alimentary tract alone, an examination of at least the kidney and urine and liver being indispensable. (From *Jour. of Lab. and Clinical Med., St. Louis*, 5: No. 5 (Feb. 1920); through *Jour. Amer. Med. Assoc.*, Mar. 27, 1920.)

**BOTULISM.**—Three different outbreaks of botulinus poisoning in Kiel within a year, which resulted in three deaths, induced Bitter to study into the question. The eating of salted herring caused the first of the three fatal cases. The herring had a typical rancid odor, and *Bacillus botulinus* was cultivated from two herring. Others fed to mice exerted a toxic effect. Too little vinegar had been used in preserving them, the pickle containing only 0.6 per cent. acetic acid. Experimentation showed that botulinus strains of various origin grew almost unchecked in nutrient agar containing up to 0.1 per cent. acetic acid. It was found, however, that a pickle containing 2 per cent. or more of acetic acid would prevent the development of poison from *B. botulinus*. It has also been shown that a 10 per cent. brine, such as is usually employed, will protect food preserved in it against the botulinus. The second outbreak in Kiel, comprising four cases, resulted from the eating of rancid-smelling raw ham. There were no fatalities, although the cases were typical and severe. In the third outbreak three persons were affected by eating salted herring, and two of these died. Bitter recommends that in the case of meat, fish and sausage poisoning all manifestations resembling botulism should be made reportable by law. He places the case mortality from botulinus poisoning in Germany at 16 per cent. Greater publicity should be given to the fact that if preserved vegetables and meats have a peculiar disagreeable odor, taste or appearance there is great danger in their consumption, and that if they are used, though they look suspicious,

they should be thoroughly cooked, though it is true that cooking sometimes fails to protect. As a rule, *B. botulinus* is found only in food carelessly preserved or stored in too warm a place. Bitter knows of only one instance in which *B. botulinus* has been isolated from other than damaged foods. Kempner and Pollock succeeded in isolating *B. botulinus* from the feces of pigs. (From *Deutsche medizinische Wochenschrift, Berlin*, 45: No. 47 (Nov. 20, 1919); through *Jour. Amer. Med. Assoc.*, Mar. 27, 1920.)

MICRO-ANALYSIS OF THE BLOOD.—Feigl suggests other lines in which Bang's micromethod can be instructively applied, with slight modifications, as in Ljungdahl's research on volatile substances in the blood. The latter uses capillary tubes for the weighing procedure, instead of Bang's paper, for determination of the acetone in the blood. This capillary technic has a certain number of advantages for research of different kinds in this line, especially for analysis of lipoids. Instead of Bang's paper, Feigl uses asbestos fibers. They take up the blood as well as the paper, and allow estimation of the ash and even of its separate elements. Extremely small quartz beakers with platinum loops, and platinum iridium beakers—eventually filled with loose quartz—also answer the same purpose. Another field for research is with microcolorimetry. Feigl has succeeded in this way with extracts from as little as 200 Mg. of blood. Determination of cholesterol is possible also with this technic. Picric acid reduction of sugar is another progress. In short, he concludes, "the reactive instrumental and theoretical possibilities of colorimetry and the wonderful nephelometric findings open prospects of applying Bang's fundamental principle in untried fields which promise great progress." (Nephelometry is the method of analysis by measuring the brightness of light reflected by particles in suspension in a tube.) (From *Zentralblatt für innere Medizin, Leipzig*, 41: No. 2 (Jan. 10, 1920); through *Jour. Amer. Med. Assoc.*, Mar. 27, 1920.)

ADULTERATION OF ORIGANUM MAJORANA.—*Origanum Majorana* is characterized by numerous multicellular hairs mostly curved and usually finely warty. *Thymus serpyllum* has but few multicellular hairs; distinctive for this plant are the very short tooth-like hairs on the margin of the leaf. *T. vulgaris* has numerous short, one-celled, minutely warty hairs, and also two-celled hairs with a bent

terminal cell. The powdered leaves of *O. majorana* have been adulterated with the two last-named, and as they are difficult to distinguish, the above characters may be useful. (Griebel and Schaefer, *Pharm Ztg.*, 64: p. 784; through *The Pharm Jour. & Pharm.*, Mar. 6, 1920.)

ACTIVE PRINCIPLES OF PITUITARY GLAND.—A method of preparing crystalline residues, very active physiologically, from extracts of the posterior lobe of the pituitary gland is described by Dudley. It consists in extraction of the dried and powdered infundibulum with acidulated water, treatment of the solution with colloidal ferric hydroxide and subsequent continuous extraction of the filtrate with butyl alcohol at reduced pressure. This extract yields a crystalline residue which contains all the uterine stimulant, together with some of the pressor principle and contaminating substances. Dudley claims the uterine stimulant and histamin are not indetical, as suggested by Abel and Kubota, but are two distinct chemical substances. The only point of similarity observed is that both are readily extracted from alkaline solution by butyl alcohol. The pituitary uterine stimulant is more readily extracted from acid solution than the pressor principle. (From *Jour. Pharmacology and Exper. Therapeutics*, Baltimore; through *Jour. Amer. Med. Assoc.*, March 6, 1920.)

ANTHELMINTIC ACTION OF BENZYL ALCOHOL AND BENZYL ESTERS.—Experiments were made by Macht on both earthworms and roundworms of the pig with benzyl alcohol, benzaldehyde, benzyl acetate and benzyl benzoate. It was found that all of these drugs exerted a toxic effect on the worms but not in the same degree. The least effective was benzyl benzoate. Its weak action, however, must be for the most part due to its poor solubility and penetrating power. Benzyl alcohol was found to be the most powerful anthelmintic of the drugs studied. A 0.5 per cent. solution of it, and even weaker solutions, killed earthworms rapidly. Benzaldehyde came next in its efficiency and benzyl acetate was third. (From *Jour. Pharmacology and Exper. Therapeutics*, Baltimore; through *Jour. Amer. Med. Assoc.*, March 6, 1920.)

TOXICOLOGY OF HYDROCYANIC ACID.—Chelle reports experimental research which demonstrated that hydrocyanic acid and the alkaline cyanides become transformed under the influence of putre-

faction processes into sulphocyanic acid. This is reversible under the action of a suitable oxidizer. After the death of a dog that had died ten minutes after taking 20 Cc. of a 1 per cent. solution of potassium cyanide, the organs were examined for hydrocyanic acid the second hour, and the eighth and thirteenth day. It had all disappeared, having become transformed to sulphocyanic acid, but it was easily transformed back again. This may prove useful in suspected cases of hydrocyanic poisoning. (From *Jour. de Medecine de Bordeaux*; through *Jour. Amer. Med. Assoc.*, March 6, 1920.)

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### BOOK REVIEWS.

#### TRANSACTIONS OF THE COLLEGE OF PHYSICIANS OF PHILADELPHIA FOR THE YEAR OF 1918.

This is an interesting work containing twenty-one papers read before the members of the College of Physicians, and also the *Proceedings* of the Sections on Ophthalmology and Industrial Medicine and Health. An interesting paper is by Dr. Victor G. Heiser, member of the American Red Cross Commission to Italy, on "Some of the Accomplishments of the Italian Medical Men in the War."

To those who know Italy largely through the poor immigrants coming to this country, this account of the completeness and high efficiency of the Medical Corps of the Italian Army will be a surprise, in fact the medical corps of our own army could possibly learn much from this report. Some idea of the magnitude of work performed is shown by the fact that the hospital service of Italy expanded in two years to 1,000,000 beds, while in the whole of our own country are only 300,000 beds. The location of some of the military hospitals was an object of interest, one was located at the very front, thirty to forty feet underground. It was supplied with artificial ventilation and modern hospital furniture, with wards and a good operating room. Another was 6,000 feet above the level of the sea, hewn out of the side of a cliff, it contained thirty beds. After emergency treatment the soldiers were forwarded to the railroad by carriages suspended from wire cables passing over chasms thousands of feet deep. The improvement in lung surgery in the Italian Army has been marvellous, a leading officer thought it possible to keep down the mortality from gunshot wounds of the chest to 5 per cent.



Dr. James M. Anders has given a very interesting memoir of Dr. Samuel Gibson Dixon who filled so brilliantly for twelve years the position of Health Commissioner for the State of Pennsylvania. He organized the department, having been appointed the first commissioner by Governor Pennypacker, who was well acquainted with his ability.

At the time of his appointment he was President of the Academy of Natural Sciences which office he held for twenty-one years. Possessed of an excellent education acquired both in this country and in Europe, he was well qualified for this new position.

To give an idea of his unceasing efforts in behalf of public health we mention the following bureaus into which the department was organized: Bureau of Vital Statistics, also that of Medical Inspection; Sanitary Engineering; Division of Laboratories; Distribution of Biological Products; Accounting and Purchase of Supplies; Tuberculosis Dispensaries and Sanatoria; Bureau of Housing; The Division of Public Service, the Control of Narcotics; and that of Child Hygiene, and lastly a Division for the treatment of Social Diseases.

Much of Dr. Dixon's best energies and closest supervision was devoted to the organization and planning of the tuberculosis work of the state. Dr. Chas. W. Burr has furnished a most interesting biography of Jean Paul Marat, physician, revolutionist and paranoic. He was one of the three monsters (Marat, Robespierre and Danton), who incited and pushed the French Revolution in such a heartless manner, shedding the blood of many of the bravest and ablest sons and daughters of France. "Marat wanted to be a leader. He believed he could rule the country if only enough people were killed. He was shrewd enough to know that if he shouted long enough and loud enough that he was the people's friend, that many would believe and follow him.

"His creed was simple, all that the rich own belongs to the poor because they stole it from the poor. His theory of government was equally simple. If you don't agree with me you are not a patriot, if you are not a patriot the proper punishment is death. Therefore we will kill everybody who disagrees with us and then we will have the millenium, the brotherhood of man." He came to an end, none too soon, by the dagger of Charlotte Corday for he had caused France to wade through rivers of blood.

This volume is a book of 300 pages, well printed and bound, a credit to the College of Physicians. C. B. LOWE, M.D.

## SOUTH CHINA CAMPHOR TRADE.\*

BY CONSUL GENERAL GEO. E. ANDERSON, HONGKONG, DEC. 12, 1919.

The interesting demand from the United States for supplies of camphor from South China is leading to a very marked activity on the part of all interests concerned in the trade and there is every indication that there will be a very large development in the volume of the output from both Kwangtung and Fukien Provinces, where there has always been more or less activity in camphor production when there has been a favorable market, and also in Kwangsi Province, where the production heretofore has been of less importance.

The government officials of Kwangsi Province at Kuelin have organized a company for the exploitation of the industry and have established a factory at that provincial capital with a view to eventually placing the industry on a modern basis by the introduction of modern methods, although for the time being the gum is being distilled by the old Chinese processes which give an impure product and are wasteful. In other respects the production and export of the gum are being organized in an effective way.

*Exports of Camphor to United States—Camphor Oil.*—The export of the gum from Hongkong is continuing on a large scale. Exports to the United States during the month of November amounted to 164,575 pounds valued at \$309,719, and the total exports to the United States for the year to date are valued at \$1,844,391. An effort is now being made by buyers representing American concerns to establish a trade in camphor oil, which usually contains about 60 per cent. of pure camphor, as well as other valuable constituents. Camphor oil is already being exported in a considerable volume from the Kwangtung, Fukien and Kiangsi field by way of Kiukiang and the Yangtze valley. It is exported in cases containing two old kerosene tins, which hold about 65 pounds to the case. The oil, as well as camphor, in the northern field, has been controlled to a greater or less extent by Japanese firms heretofore.

Native reports indicate that the best untouched camphor tree field in China is in Kiangsi Province, though the trees in Kwangsi Province have been cut out comparatively little. Great interest has been shown by a number of investigators in the island of Hainan, where the possibilities of camphor production, both from indigenous trees and from planted groves, are being looked into.

\* From *Commerce Reports*, Feb. 11, 1920.

# THE AMERICAN JOURNAL OF PHARMACY

MAY, 1920

JUN 14 1920

EDITORIAL.

## A NEW LAW COVERING THE SALE OF DISTILLED SPIRITS AND WINES FOR MEDICINAL PURPOSES ENACTED IN NEW JERSEY.

At this year's session of the New Jersey legislature the following law was enacted and having received the approval of the Governor will become operative on July 4th.

AN ACT to restrict the sale at retail of distilled spirits and wines for medicinal purposes to bona fide prescriptions and to define the prescribing and dispensing of these as in performance of professional duty and not in violation of prohibition enactments.

BE IT ENACTED *by the Senate and General Assembly of the State of New Jersey:*

1. On and after the passage of this act, it shall not be lawful for any druggist, except a pharmacist registered as such in accordance with the law of this State and engaged at the time in the actual practice of pharmacy, to sell at retail distilled spirits and wines and

the sale shall be made only on a bona fide prescription written by a licensed practitioner of medicine engaged at the time in the practice of his medical profession. Distilled spirits and wines may be prescribed by such medical practitioner when in good faith he believes that the use of alcoholic liquors as a medicine is indicated and only after a personal physical examination of the patient or after consultation with another practitioner who has made a personal physical examination of the patient, and the prescription shall be written in duplicate, the prescriber retaining one copy, and there shall be written thereon the name and address of the patient for whom prescribed, and the name and address of the prescriber, and the prescription shall not be filled more than once, and there shall not be prescribed for the same patient for internal administration more than one pint of distilled spirits within any period of ten days, and the liquor prescribed can be consumed only by the patient named in the prescription, and the pharmacist filling the prescription shall preserve it for at least two years on a separate file kept for prescriptions for distilled spirits and wines, and all such files and records shall be open at all time to the inspection of any authorized officer of the law.

2. The prescribing and dispensing of alcoholic liquors on bona fide prescriptions in accordance with the provisions of this act shall be deemed and is hereby defined as in performance of the professional duty of the medical practitioner and the pharmacist, and the pharmacist shall not by reason of such professional duty be classified as a dealer in alcoholic beverages nor shall he be subject to the license fees that are exacted of dealers in alcoholic beverages, nor shall the dispensing of alcoholic liquors in the discharge of his professional service be construed as violating the provisions of the enactments of this State or of any political subdivision thereof enacted for the purpose of restricting and controlling the sale and use of alcoholic liquors as beverages and commonly spoken of as local option and prohibition laws; *provided*, that nothing in this act shall be construed as preventing the sale and use of alcohol when properly medicated and sold in accordance with the regulations of the Bureau of Internal Revenue of the Treasury Department of the United States nor with the manufacture, sale and use of denatured alcohol, nor with manufacture, sale and use of wines for sacramental and like religious rites in accordance with the Federal statutes.

3. Any person violating any of the provisions of section one of

this act shall be guilty of a misdemeanor and upon conviction shall be subject to a fine of not more than one hundred dollars, and any medical practitioner or any pharmacist who is convicted more than once of violating the provisions thereof may have his license to practice in this State revoked.

This act was designed to serve several purposes all of which we believe will be to the benefit of the professional practice of pharmacy. It aims to prevent the unscrupulous medical practitioner or druggist engaging in the nefarious "booze business." It restricts the sale of distilled spirits and wines for medicinal purposes to prescriptions written in good faith by the physician in attendance when indicated by the physical condition of the patient. In harmony with the Federal statute and regulations, it limits the amount that can be so dispensed and prescribes the procedures that must be followed by both physician and pharmacist. The penalties provided for violating any of the provisions relating to dispensing should be sufficient to deter any one from such infraction, as he becomes liable to a fine for each irregularity of this type and further upon more than one conviction for such offenses the physician or pharmacist may have his license to practice in the State revoked.

Under the existing laws and regulations of the U. S. Treasury, every pharmacist who dispenses distilled spirits or wines, even though such dispensing be done only on bona fide prescriptions, becomes a retail liquor dealer and must qualify and pay the stamp tax as such before dispensing any prescriptions for these or for pure alcohol intended for external application.

Paragraph 12, Sec. 1001 of the Revenue Act of 1918 pro-

vides further that "every person carrying on the business of retail liquor dealer in any state, territory, or district of the United States contrary to the laws of such state, territory, or district, or in any place therein in which carrying on such business is prohibited by local or municipal law, shall pay, in addition to all other taxes, special or otherwise, imposed by existing law or by this act, \$1,000."

In many sections of New Jersey local option laws have been adopted and as these, as a rule, do not exempt pharmacists in the dispensing of prescriptions for liquors, it is apparent that in such districts the pharmacist who wished to qualify to fill such bona fide prescriptions would be prevented by the prohibitive tax of \$1,000 plus the normal Federal Stamp Tax of \$25 paid by the pharmacist situated in a nearby municipality where a local option law had not been adopted. It is manifestly unfair to the patients that they should not be able to have their medical needs supplied near home and also that such discrimination should exist between pharmacists engaged in business in the same State.

One of the prime objects of this law was to provide for the exemption of pharmacists in the dispensing of distilled spirits and wines needed for strictly medicinal purposes from the provisions of local option or prohibition laws already enacted in the State or subdivisions thereof. By this act, such legitimate prescribing and dispensing is defined as coming within the professional duties of the physician and the pharmacist and the latter is exempted by the State from the odium of being classified as a dealer in alcoholic beverages and from the license fees and penalties exacted under these laws. Under this construction, the pharmacist in dispensing in accordance with the provisions of the act, which to all intents and purposes are the same as those of the Volstead Act, *is not carrying on the business of a retail liquor dealer contrary to laws of the State or place therein*

*in which carrying on such business is prohibited by local or municipal law and, consequently, he should not have to pay the additional tax of \$1,000 as provided by the Revenue Act of 1918.*

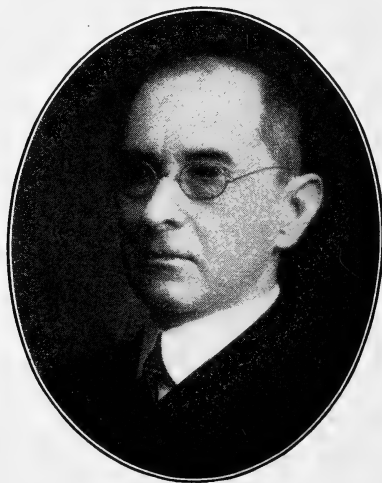
The law enacted in New Jersey may possibly serve as a model for similar enactments in other states where prohibition laws act as barriers to the necessary dispensing of such medicines.

G. M. B.

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#### TESTIMONIAL DINNER FOR JOHN URI LLOYD.

The bestowal of the Remington Honor Medal in Pharmacy for the second time was made the occasion for a testimonial dinner in honor of Prof. John Uri Lloyd, the recipient. The presentation was at an adjourned meeting of the New York Branch of the A. Ph. A. held at Hotel Pennsylvania, New York, on Monday evening, April 19. Nearly one hundred representative pharmacists from New



JOHN URI LLOYD, PH.M.

York, Pennsylvania and New Jersey gathered at this function to do honor to the guest of the occasion.

Prof. William C. Anderson presided and acted as toast master. The presentation was made in a masterly address by Dr. Jacob Diner, who reviewed the impressions that the work of Professor Lloyd had very early in his own pharmaceutical career made upon



him and the widespread influence that the scientific investigations and literary contributions of this eminent worker had exerted in fields that were at times beyond the boundaries of pharmacy. Notably among such was his early contributions and researches on colloidal chemistry which were now being fully recognized as among the original and fundamental studies in this interesting branch of chemistry.

In responding Professor Lloyd announced that this was his seventy-first birthday and that but for this event he should have been at home enjoying the felicitations of his home circle. He was in one of his most happy moods and delightfully reminiscent and in his own inimitable manner gave his audience an insight into his early induction into the trials and tribulations of the embryo pharmacist of nearly sixty years ago and the difficulties that he experienced in learning the art of the apothecary. He referred to the unexpected incidents in his early career that had impelled him to continue in pharmacy and how these had led him up to this occasion and the honor, which he believed would not have come to him except through the guidance of the unseen influence and the preordination of the unexpected events depicted that had determined his future.

Among others who briefly responded, at the toastmaster's request, and voiced in appropriate remarks their tributes and appreciation of the life-time research studies of Professor Lloyd were Dean Charles H. La Wall, President Edward A. Sayre, of the New Jersey Pharmaceutical Association, Editor E. G. Eberle of the *Journal of the American Pharmaceutical Association*, President Robert S. Lehman, of the New York State Pharmaceutical Association, Professor Charles Baskerville of New York, and George M. Beringer of Camden, N. J.

Regrets at unavoidable absence were received from Professors Henry H. Rusby and E. Fullerton Cook.

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## A CONTRIBUTION TO THE PHARMACOLOGY OF COTTON ROOT BARK.

BY CHARLES R. ECKLER, M.S.

### PURPOSE.

Cotton root bark has been used as a medicine for many years by the negroes of the South, and it is stated that they brought the knowledge of the drug with them from Africa. The drug has been

used as a substitute for ergot by some physicians who have claimed that its action resembles that of ergot, and that it has the advantage over the latter of being safer and more stable. This use of cotton root bark has been very largely of an empirical nature, for very little experimental work on animals has been reported and the most of this has seemed unfavorable to the use of the drug. The majority of the clinical reports have also seemed unfavorable. At a comparatively recent date, however, J. C. Scott published a favorable report regarding the action on the cat's uterus.<sup>1</sup> This author states that "gossypii cortex is stable and very active." In the two experiments which he reports, one on the isolated and one on the intact uterus, he seems to have used a powdered extract of the root bark suspended in Ringer's solution, which, in the case of the isolated uterus was applied directly to the organ, and in the case of the intact uterus was apparently given intramuscularly. It became of interest, therefore, to know more about the activity of cotton root bark, as compared with that of ergot in particular, and to some extent with that of pituitary extract. It became of interest, also, to learn whether or not there was any distinct difference in activity between the "green" and the "dried" bark of commerce, and whether or not drug collected at the time of flowering would be more active than the commercial drug which is, in either the case of the "green" or the "dried," collected after the cotton is harvested, and further, whether or not different varieties of the cotton plant would show any distinct difference in activity. The purpose of this work was to gain more definite knowledge regarding these points.

#### MATERIAL.

Several commercial samples of "green" and "dried" root bark were tested, and in addition, samples of thirteen different varieties of the cotton plant. The latter were carefully collected at the time of flowering. They were obtained by Mr. F. A. Miller, of our botanical department, from the Georgia Agricultural Experiment Station. Fluidextracts or modified fluidextracts of the drug, only, were tested. Aqueous suspensions of powdered extract were not employed. A part of the commercial "dried" barks were extracted with a menstruum of alcohol and glycerin, 3 to 1, and a part with 75% alcohol. The "green" barks were extracted with the alcohol-glycerin, and the thirteen samples were extracted with 75% alcohol.

Fluidextracts of ergot were used for comparison. These were

made from commercial lots of drug, by extraction with 50% alcohol.

The pituitary extracts used in comparative tests were either samples of commercial extract, or laboratory extractions of commercial lots of glands.

#### METHODS.

It was decided to test the activity of cotton root barks by the methods commonly employed for the testing of ergot, namely, the cock's comb, blood pressure, and uterus methods. These methods as carried out in this work are briefly as follows:

##### COCK'S COMB METHOD.

The cock's comb method consists in administering to pure-bred, single-comb, white leghorn roosters, by injection into the pectoral muscles, gradually increasing or diminishing doses of fluidextract until a slight but distinct and unmistakable bluing of the comb points has been produced. This method is simple and rapid, and has been reported as giving results which seem to run closely parallel to those obtained by the intact uterus method. Perhaps no other method is so commonly employed for the testing of ergot. The end-point, unlike that of the other methods, is a purely visual one.

##### BLOOD PRESSURE METHOD.

The blood pressure method consists in recording the change in carotid pressure caused by the intravenous injection of the fluidextract by way of the saphenous vein. Young, medium sized dogs are the subjects preferred. These have seemed to give the most satisfactory records when anaesthetized with morphine sulphate (0.010 to 0.012 G. per Kg.) and hyoscine hydrobromide (0.000,064 to 0.000,128 G. per Kg.). Ether is used for the operation of inserting cannulae, etc., but is withdrawn as soon as the apparatus is set up and running. Artificial respiration is established in all cases. The common mercury manometer was employed in this work. The doses of fluidextract, calculated per Kg. of body weight, were diluted for injection with one or two times their volume of salt solution.

A few experiments were carried out on decapitated dogs and cats, prepared according to the method of Sherrington.<sup>2</sup>

The blood pressure method, essentially as described, is a commonly employed laboratory method for studying the effect of drugs on the circulation. It has been used extensively for determining the pressor effect of preparations of ergot.

## THE ISOLATED UTERUS METHOD.

The isolated uterus method consists in recording the movements of isolated horns of the virgin guinea pig's uterus. These muscular segments are kept bathed in warm, oxygenated Locke's solution, and at intervals the drug to be tested is added to the Locke's solution in quantitative manner. The segment being attached to a writing lever, any contractions or relaxations caused by the application of the drug are recorded on a smoked surface. (A more detailed description of the method and apparatus may be found in *THIS JOURNAL*, 89: 195, 1917; and in the *Jour. Lab. and Clin. Med.*, 2: 819, 1917.)

The isolated uterus method is commonly employed for determining the value of pituitary extracts. The method is also used for testing ergot and other drugs which cause, by their application, a change in the contractility of involuntary muscle.

## THE INTACT UTERUS METHOD.

The intact uterus method consists in recording the movement of the uterus in situ caused by the intravenous injection of the drug, usually by way of the jugular vein. The animal, anaesthetized with one of the soporific drugs such as acetoform or paraldehyde, is partly immersed in a saline bath of body temperature. The uterus is exposed under the salt solution and attached to a Cushny single myocardiograph or similar instrument, which records, on a smoked surface, any movement of the organ.

The intact uterus method is a very useful one for studying the qualitative action of those drugs which are used in medicine for their effect on this organ. It seems to be the most logical one for this purpose. As a method of quantitative assay, where many injections have to be made, it is perhaps less serviceable than the isolated uterus method, for the factors governing the uterus are less under control and the organ is influenced to a greater extent by the cumulative action of previous doses of the drug.

## RESULTS OF COCK'S COMB EXPERIMENTS.

The fowls to be used for the testing of cotton root bark were either given, or had been given, doses of ergot. The results of these tests were desired to serve as a control. Fowls

vary in their resistance to drugs and occasionally, although rather rarely, one will find combs which do not become distinctly blue after ergot, the effect being more of a blanching. These control tests showed that the combs could be blued by small to medium doses of ergot.

TABLE 2. COCK'S COMB TESTS ON COTTON ROOT BARK.

A fluidextract of commercial, dried cotton root bark, made with a menstruum of alcohol and glycerin (3 to 1), gave the following results on the fowls previously tested with ergot:

Fowl	Weight in Kg.	Dose per Kg.	Results
394	1.545	1.0 c.c.	No noticeable bluing of comb
386	1.544	1.0 c.c.	" " " " "
388	1.460	1.5 c.c.	" " " " "
393	1.388	2.0 c.c.	" " " " "
397	1.665	2.0 c.c.	" " " " "
384	1.705	2.5 c.c.	" " " " "
388	1.467	2.5 c.c.	" " " " "
391	1.661	3.0 c.c.	" " " " "
396	1.706	3.0 c.c.	" " " " "
398	1.690	3.0 c.c.	" " " " "
400	1.507	3.0 c.c.	" " " " "
501	1.644	3.0 c.c.	Very faint bluing of comb
502	1.553	4.0 c.c.	Extremely faint bluing of comb
503	1.532	5.0 c.c.	Faint bluing of comb

A fluidextract of commercial, "green" cotton root bark, made with a menstruum of alcohol and glycerin (3 to 1), gave results as follows:

Fowl	Weight in Kg.	Dose per Kg.	Results
511	1.703	1.0 c.c.	No noticeable bluing of comb
515	1.532	1.0 c.c.	" " " " "
512	1.586	2.0 c.c.	" " " " "
516	1.688	2.0 c.c.	" " " " "
530	1.630	2.0 c.c.	" " " " "
514	1.441	3.0 c.c.	" " " " "
517	1.337	3.0 c.c.	" " " " "
524	1.498	3.0 c.c.	" " " " "
518	1.576	3.0 c.c.	" " " " "
511	1.635	3.0 c.c.	" " " " "
512	1.578	3.0 c.c.	" " " " "
515	1.528	3.0 c.c.	" " " " "
516	1.662	3.0 c.c.	" " " " "
385	1.715	3.0 c.c.	Extremely faint bluing of comb

The commercial drug did not, in any case, produce bluing of the cock's comb in doses smaller than 3 c.c. per Kg. The dose of ergot required for these same fowls was from 0.50 to 1 c.c. Other symptoms were evident, however, such as blanching of the comb, wattles, and areas about the eyes, drooping of the feathers, dyspnoea and diarrhoea. With doses of 4 and 5 c.c. per Kg. the fowls seemed very sick, and while slight bluing was produced, the end point was so indefinite that a quantitative assay by this method seemed to be quite impossible. Doses of 2 and 3 c.c. per Kg. of each of the thir-

teen samples were then given to fowls, the combs of which had previously been blued by small doses of ergot. From the results shown in Table 3 it may be seen that none of the thirteen samples were distinctly active in bluing the comb in doses of 3 c.c. per Kg. This dose is four times the amount which was required of fluidextract of ergot to produce a distinct bluing in the same fowls. Testing by the cock's comb method was therefore discontinued.

Table 3  
Tests on Samples of Different Varieties of  
Cotton Root Bark, Collected at Flowering  
*Cock's Comb Method*

Sample	Fowl	Weight	Dose per Kg.	Results					
No. 1	540	2.000	2 c.c.	No noticeable bluing of comb.					
	544	1.713	3 c.c. <td>"</td> <td>"</td> <td>"</td> <td>"</td> <td>"</td> <td>"</td>	"	"	"	"	"	"
No. 2	535	1.424	2 c.c.	"	"	"	"	"	(?) (Cold)
	548	1.785	3 c.c.	"	"	"	"	"	"
No. 3	545	1.921	2 c.c.	"	"	"	"	"	(Redder)
	540	1.404	3 c.c.	"	"	"	"	"	"
No. 4	541	1.852	2 c.c.	"	"	"	"	"	(Redder)
	541	1.923	3 c.c.	"	"	"	"	"	"
No. 5	554	1.703	2 c.c.	"	"	"	"	"	(Redder)
	535	1.547	3 c.c.	"	"	"	"	"	"
No. 6	548	1.908	2 c.c.	"	"	"	"	"	Warm red
	545	1.924	3 c.c.	"	"	"	"	"	
No. 7	540	1.957	2 c.c.	"	"	"	"	"	(?) (Cold)
	541	1.981	3 c.c.	"	"	"	"	"	(?) (Cold)
No. 8	541	1.859	2 c.c.	"	"	"	"	"	(?) (Cold)
	540	2.106	3 c.c.	"	"	"	"	"	(?) (Cold)
No. 9	545	1.871	2 c.c.	No noticeable bluing of comb.					
	548	1.776	3 c.c.	"	"	"	"	"	(?) (Cold)
No. 10	545	1.342	2 c.c.	"	"	"	"	"	(?) (Cold)
	544	1.746	3 c.c.	"	"	"	"	"	
No. 11	535	1.342	2 c.c.	"	"	"	"	"	(?) (Cold)
	535	1.584	3 c.c.	"	"	"	"	"	
No. 12	544	1.678	2. cc.	"	"	"	"	"	(?) (Cold)
	539	1.716	3 c.c.	"	"	"	"	"	
No. 13	548	1.866	2 c.c.	"	"	"	"	"	Extremely faint bluing of comb (?)
	546	1.775	3 c.c.						

In the cases marked (?) there seemed to be a mere suggestion of bluing, so faint, however, that it could not be distinguished with certainty. No. 13 with 3 c. c. was the most pronounced of these.

#### BLOOD PRESSURE EXPERIMENTS.

Before presenting the results of blood pressure experiments on cotton root bark, results of normal blood pressures of anaesthetized dogs were observed in order to determine with what regularity the normal pressure would run when recorded by the method and apparatus employed. Such results may be seen in Table 4. Slight variations in pressure would probably be recorded with the best of apparatus and under the most careful technic. Occasionally, however, more pronounced changes may be caused by a slight movement of the animal as happened in experiment 786. A somewhat more

disturbing change is such as may be seen in experiment 788, where there is for some little time a slight but gradual fall in pressure, and in 779, where there is a slight but gradual rise. In both cases, however, the pressure ran with fair uniformity after the 10 minute period. In experiment 767 a slight rise appears after the 20 minute period. No cause can be assigned for these changes except by supposing that the force or rate of the respiration was not such as to quite accommodate the needs of the particular animals. These points should be considered when viewing Table 6, 6A and 6B, which show the results of blood pressure experiments on cotton root bark. Three of the kymograms may be seen, also, in Chart 1.

Table 4  
Records of Normal Blood Pressures of Dogs  
(Morphine-Hyoscine Anaesthesia)  
Pressure given in millimeters  
Kymograms

Time	767 Dog 10.2 Kg.	773 Dog 8.3 Kg.	788 Dog 11.6 Kg.	775 Dog 6.2 Kg.	779 Dog 19.3 Kg.	786 Dog 10 Kg.
Start	110	119	148	125	104	123
5'	108	120	138	115	117	120
10'	110	127	135	106	127	117
15'	110	124	132	105	133	114
20'	109	125	130	105	133	120
25'	116	122	130	105	134	animal
30'	116	122	129	106	135	moved
35'	119	118	127	119	134	141
40'	122	117	126		134	139
45'	122	118	126		134	135
50'	122	118	128		134	
55'	120	114	127		138	
60'	118	116			138	
65'	115	115			138	
70'	113	115				
75'	112	118				
80'	109					
100'	111					
115'	107					

A few blood pressure tracings were made, showing the effect of ergot, in order to compare the action of cotton root bark with that of ergot on the circulation, and to show how extensively the normal pressure may be influenced. Table 5 shows the results of six ergot blood pressure experiments and gives one a fair idea of the great elevation in pressure which is almost invariably produced by carefully prepared fluidextracts of this drug.

Table 5  
Blood Pressure Records on Samples of Fluid Extract of Ergot, Taken on Dogs

Dog Wt. in Kg.	Dose per Kg.	Normal Pressure	Pressure at Periods After Injection of Drug							
			1-3'	5'	10'	15'	20'	25'	30'	
12.7	.05 c.c.	147	225	218	187	187	185	178	174	
10.6	.05 c.c.	147	237	226	206	195	189	188	185	
14.4	.05 c.c.	150	214	214	200	176	167	(150at42')		
6.6	.10 c.c.	144	263	220	204	190	188	181		
10.5	.10 c.c.	129	175	198	190	184	182	180		
22.2	.10 c.c.	144	190	172	220	234	220	216	210	

*Table 6*  
*Blood Pressure Records of Thirteen Samples of*  
*Cotton Root Bark on Dogs*

Drug	Dose per Kg.	Pressure at Start	Pressure at Periods After Injection						
			1-3'	5'	10'	15'	20'	25'	20'
(Kymogram 736. Dog Wt. 12 Kg. Morphine S.-Hyoscine HBr. anaesthesia.)									
Cotton R. No. 1	.1 c.c.	120	124	118	clot	104			
	.2 c.c.	100	116	107	114	114			
F. E. Ergot	.05 c.c.	115	153	131	133				
(Kymogram 772. Dog Wt. 10.5 Kg. Morphine S.-Hyoscine Hbr.)									
Cotton R. No. 1	.05 c.c.	135	138	135	132	130			
	.1 c.c.	130	142	clot	130	134	134		
	.2 c.c.	127	145	123	126				
(Kymogram 773. Dog Wt. 8.3 Kg. Morphine S.-Hyoscine HBr.)									
Cotton R. No. 1	.2 c.c.	117	133	117	114				
F. E. Ergot	1. c.c.	114	133						
(Kymogram 741. Dog Wt. 8.8 Kg. Morphine S.-Hyoscine Hbr.)									
Cotton R. No. 2	1 c.c.	137	147	142	145	152	157		
	.2 c.c.	157	168	153	153	clot			143
F. E. Ergot	.05 c.c.	143	158	179	164	162			
(Kymogram 778. Dog Wt. 11.6 Kg. Morphine S.-Hyoscine HBr.)									
Cotton R. No. 2	.2 c.c.	127	137	130	126	124			
F. E. Ergot	.05 c.c.	124	140	140	140				
	.05 c.c.	140	155	148	154				
(Kymogram 778-A. Dog Wt. 11.7 Kg. Morphine S.-Hyoscine HBr.)									
Cotton R. No. 3	.1 c.c.	105	117	108	108	104	103		
	.2 c.c.	103	122	106	clot	127	119		
F. E. Ergot	.05 c.c.	122	149	134	129				
(Kymogram 743. Dog Wt. 8 Kg. Morphine S.-Hyoscine HBr.)									
Cotton R. No. 3	.2 c.c.	126	135	118	118	119	113		
	.3 c.c.	113	120	105	108	109	112		
F. E. Ergot	.05 c.c.	113	134	129	131	137	133	133	
	.1 c.c.	133	160	144					
(Kymogram 779. Dog Wt. 19.3 Kg. Morphine S.-Hyoscine HBr.)									
Cotton R. No. 3	.1 c.c.	138	152	138	140	140			
(Kymogram 749. Dog Wt. 10 Kg. Morphine S.-Hyoscine HBr.)									
Cotton R. No. 4	.1 c.c.	113	128	121	125	124	126	124	
	.2 c.c.	124	146	123	131	133			
(Kymogram 750. Dog Wt. 9.4 Kg. Morphine S.-Hyoscine HBr.)									
Cotton R. No. 5	.1 c.c.	125	144	135	132	130	130	130	
	.2 c.c.	130	148	143	136	133	134		
F. E. Ergot	.05 c.c.	141	198	195	166	166	150	153	
(Kymogram 751. Dog Wt. 5.9 Kg. Morphine S.-Hyoscine HBr.)									
Cotton R. No. 6	.1 c.c.	149	152	144	150	155	154	154	
	.2 c.c.	154	176	154	158	clot		141	
F. E. Ergot	.05 c.c.	130	176	151	154	150	141	136	
(Kymogram 753. Dog Wt. 8.8 Kg. Morphine S.-Hyoscine HBr.)									
Cotton R. No. 7	.1 c.c.	142	148	146	154	155			
	.2 c.c.	158	164	161	157	152	147	144	
F. E. Ergot	.05 c.c.	145	168	169	160	158	157		
(Kymogram 756. Dog Wt. 13.6 Kg. Morphine S.-Hyoscine HBr.)									
Cotton R. No. 8	.1 c.c.	121	137	125	122	118	120	122	
	.2 c.c.	139	153	136	138	135	132	131	
F. E. Ergot	.05 c.c.	131	164	188	187	172	166	155	
(Kymogram 755. Dog Wt. 14 Kg. Morphine S.-Hyoscine HBr.)									
Cotton R. No. 9	.1 c.c.	124	139	135	136	143	152	153	
	.2 c.c.	150	170	150	140	142	139	138	
F. E. Ergot	.05 c.c.	130	157	137	130	129	130	132	



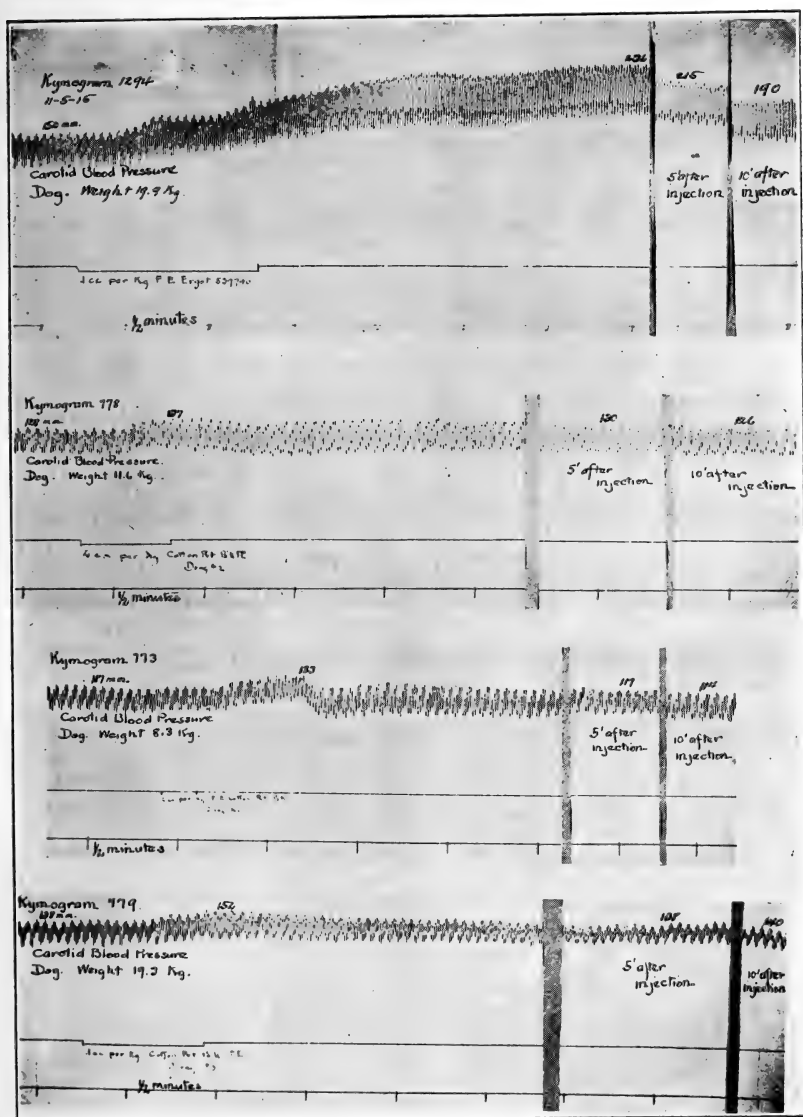


CHART I.

Kymogram 1294 shows the effect of fluidextract of ergot on the blood pressure of the dog.

Kymograms 778, 773 and 779 represent three different blood pressure experiments which show the effect of cotton root bark on the blood pressure of the dog.

Table 6  
*Blood Pressure Records of Thirteen Samples of  
Cotton Root Bark on Dogs*

Cotton Root Bark on Dogs									
Drug	Dose per Kg.	Pressure at Start	Pressure at 1-3' 5'	Periods 10' 15' 20'	After 25' 30'	Injection			
(Kymogram 759. Cotton R. No. 10)	Dog Wt. 5.5 Kg.	Morphine S.-Hyoscine HBr.)							
	.1 c.c.	134	143 130	132 129	126 120				
	.2 c.c.	120	136 128	127 131	129 127				
F. E. Ergot	.05 c.c.	127	158 145	148 145	154 157				
(Kymogram 763. Cotton R. No. 11)	Dog Wt. 11.8 Kg.	Morphine S.-Hyoscine HBr.)							
	.1 c.c.	114	125 120	117 123	120 118				
	.2 c.c.	123	132 124	121 118	118 122				
F. E. Ergot	.05 c.c.	122	140 138	136 124					
	.1 c.c.	136	157 133	124 121					
(Kymogram 764. Cotton R. No. 12)	Dog Wt. 11.2 Kg.	Morphine S.-Hyoscine HBr.)							
	.1 c.c.	112	123 135	120 120	120 117				
	.2 c.c.	117	127 123	126 117	117 140				
F. E. Ergot	.05 c.c.	118	172 170	169 152	140 140				
	.1 c.c.	127	147 137	142 142					
(Kymogram 765. Cotton R. No. 13)	Dog Wt. 8.9 Kg.	Morphine S.-Hyoscine HBr.)							
	.1 c.c.	116	124 129	128 133	133 133				
	.2 c.c.	133	147 141	137 137	137 133				
F. E. Ergot	.05 c.c.	116	140 140						

Table 6-A  
Blood Pressure Records  
of Commercial Cotton Root Bark on Dogs

Drug	Dose per Kg.	Pressure at Start	Pressure at Periods After Injection					
			1-3'	5'	10'	15'	20'	25'
(Kymogram 902. F. E. C. (Dry) 4 1/2' later =	Dog Wt. 4.7 Kg. .1 c.c. .1 c.c.	Morphine Sulphate 144 106	160 126	145 118	143 117			
(Kymogram 901. F. E. C. (Dry)	Dog Wt. 10 Kg. .1 c.c. .15 c.c. .20 c.c.	Morphine Sulphate 110 120 136	138 147 138	136 134 136	127 136 136	120 136 122	120 136 134	120 136 131
(Kymogram 900. Alcohol-glyc. (3 to 1) F. E. C. (Dry) F. E. Ergot F. E. C. (Dry)	Dog Wt. 11.8 Kg. .15 c.c. .15 c.c. .15 c.c. .20 c.c. .15 c.c. .15 c.c.	Morphine Sulphate 136 136 143 145 140 Caused death	144 136 159 158 178	145 145 145 122 170	145 141 158	140 140 158		151 149
(Kymogram 894. Adrenal-glyc. F. E. C. (Dry) F. E. Ergot	Dog Wt. 12 Kg. .2 c.c. .2 c.c. .2 c.c.	Morphine Sulphate 111 118 123	119 128 114	119 120 clot	120 114	114		
(Kymogram 893. Adrenal Ext. F. E. C. (Dry)	Dog Wt. 10 Kg. .1 c.c. .15 c.c. .2 c.c. .3 c.c.	Morphine Sulphate 116 129 110 103 101	146 138 115 110 Fall	130 114 clot 101 Slow	110 110 112 101 recovery.		95	
(Kymogram 891. Adrenal Ext. F. E. C. (Dry)	Dog Wt. 7 Kg. .2 c.c. .2 c.c. .2 c.c. .3 c.c. .15 c.c.	Morphine Sulphate 135 143 139 126 Gradual fall for 5' then slow recovery. Fall, slight rise, then gradual lowering.	157 164 150 136	143 143 120 124	143 140 117 127		123 126	



*Table 6-A*  
*Blood Pressure Records*  
*of Commercial Cotton Root Bark on Dogs*

Drug	Dog Wt.	Dose per Kg.	Pressure at Start	Pressure at Periods After Injection					
				1-3'	5'	10'	15'	20'	25'
(Kymogram 890. Adrenal Ext.)			Morphine Sulphate	143	170	140			
Alcohol-glyc.		.3 c.c.	No effect						
F. E. C. (Dry)		.2 c.c.	146	155	128	126	clot	132	122
		.3 c.c.	122	140	84	93	clot	102	107
F. E. Ergot		.15 c.c.	Slight rise, then gradual fall.						
(Kymogram 691. After Ergot.)	Dog Wt. 10.8 Kg.		Morph. S.-Hyoscine HBr.)						
F. E. C. (Dry)		.05 c.c.	125	135	130	128	125	123	122
(Kymogram 892. F. E. C. (Green))	Dog Wt. 27.4 Kg.	.2 c.c.	Morph. S.-Atropine S.)	143	154	146	146	142	144
F. E. Ergot		.1 c.c.	144	210	210	204	200	202	
(Kymogram 982. F. E. C. (Green))	Dog Wt. 11 Kg.	.2 c.c.	Morph. S.-Hyoscine HBr. Cut Vagi.)	122	144	126	127		
Alc.-glycerin		.2 c.c.	No effect						
F. E. Ergot		.05 c.c.	132	190	163	156	135	130	
F. E. C. (Green)		.2 c.c.	No effect						
(Kymogram 895. F. E. C. (Green))	Dog Wt. 2.7 Kg.	.2 c.c.	Morph. S.-Atropine S.)	112	134	132	132	134	130
		.2 c.c.	130	148	124	124	118	112	112
F. E. Ergot		.1 c.c.	112	154	138	131	120	119	119

*Table 6-B*  
*Blood Pressure Records*  
*of Commercial Cotton Root Bark on*  
*Spinal Preparations*

Drug	Preparation Wt.	Dose per Kg.	Pressure at Start	Pressure at Periods After Injection					
				1-3'	5'	10'	15'	20'	25'
(Kymogram 896. F. E. C. (Dry))	Preparation Wt. 2.2 Kg. Cat.)	.2 c.c.	82	46-69	62	67			
F. E. Ergot		.2 c.c.	17	38-138	134	126	110	100	78
F. E. C.		.2 c.c.	Abrupt fall. Heart stopped. Epinephrin was given and the heart massaged. Heart began beating. Later ergot caused a rise in pressure.						
(Kymogram 898. Alc.-glyc. (3 to 1))	Preparation Wt. 2.4 Kg. Cat.)	.16 c.c.	58	60	56				
F. E. C. (Dry)		.16 c.c.	58	48	46				
F. E. Ergot		.08 c.c.	44	grad. rise	80	75	66		
F. E. C.		.16 c.c.	64	Fall. Heart stopped. Massaging and epinephrin started heart.					
F. E. C.		.08 c.c.	Gradual fall.						
F. E. C.		.08 c.c.	Pressure fell nearly to zero, heart stopped but recovered after massaging and epinephrin.						
(Kymogram 4015. F. E. C. (Dry))	Dog preparation Wt. 7.4 Kg.)	.10 c.c.	65	70-63	56	51			
F. E. Ergot		.05 c.c.	51	65-62	66	65	61	60	
F. E. C.		.10 c.c.	60	62-59	56				
F. E. Ergot		.10 c.c.	55	63-58	60				
Pit. Ext. 1:1000		.20 c.c.	60	63-67					

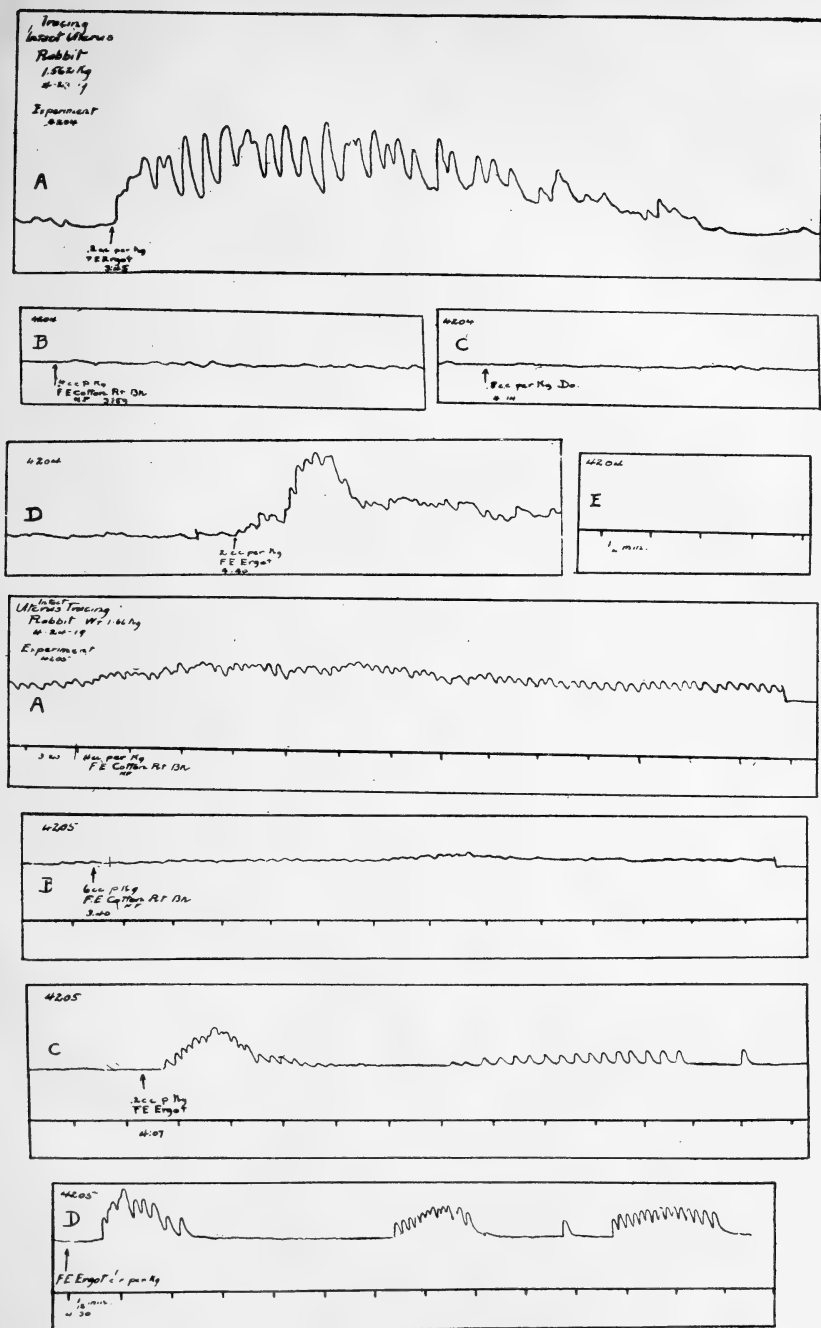


CHART 3.

This chart shows sections of the kymograms of two experiments on the intact uterus of the virgin rabbit. In experiment No. 4204, D seems to show a diminished effect of ergot as compared with A, due to the two injections of cotton root bark shown in B and C. This experiment gives an idea of the relative effect of the two drugs. In experiment 4205, B shows the effect of cotton root bark to be diminished following A, even though the dose was increased.

## COTTON ROOT BARK.

## BLOOD PRESSURE EXPERIMENTS ON THE CAT.

Four blood pressure experiments were carried out on cats. These animals were anaesthetized with acetoform. In one case 0.2 Cc. per Kg. of F. E. Cotton R. B. caused almost no effect. In the other three cases 0.1 and 0.2 Cc. doses per Kg. caused an abrupt and extensive fall, the pressure slowly regaining the normal height or slightly above the normal. Following is an example:

Pressure at start.....	86 Mm.
0.13 Cc. per Kg. F.E.C. injected.	
Pressure 1-3' after injection.....	27 Mm.
Pressure 5' after injection.....	92 Mm.
Pressure 7' after injection.....	86 Mm.

The foregoing work was completed about June 1, 1914. The following experiments were carried out during the spring of 1919.

## ISOLATED UTERUS EXPERIMENTS.

For the uterus experiments, fresh samples of commercial drug were extracted and made into fluidextracts by the N. F. method.

The isolated uterus is, in most cases, an extremely sensitive organ, easily influenced by the chemical nature of the solutions applied to it. Any considerable amount of acid, alcohol, or astringent principle in the solution applied is likely to impair the results of the experiment. Any substance to be applied to the structure should, therefore, be in a clear, neutral or nearly neutral, saline solution. Such a solution fully representing the fluidextract of cotton root bark seemed impossible, for any extensive change in the menstruum, such as would necessarily occur when the fluid was diluted in the Locke's solution surrounding the uterus, caused a precipitation of considerable extractive matter. Such a mixture, however, with its very fine, fresh precipitate, was considered preferable to a suspension of the powdered extract. The procedure employed was to dilute the fluidextract with 9 parts of saline solution, and of this 10% mixture, the doses for application were drawn off. These doses were further diluted from 50 to 100 times when introduced into the Locke's solution surrounding the uterus. The effect of any astringent matter in this dilute solution was disregarded. It would seem to be very slight if, in truth, any were exerted. According to the work of

Table 7  
ISOLATED UTERUS EXPERIMENTS  
*Guinea Pig's Uterus*  
*Commercial Drug*

Experiment or Kymo.	Drug	Dilution	Effect	(Contractions, etc.)
1	Pituitary Extract	1:300,000	85 m.m.	contraction
	Alcohol	1: 1,333	21 "	"
	"	1: 1,333	17 "	"
	Pituitary Extract	1:300,000	67 "	"
2	Pituitary Extract	1:300,000	87 "	"
	Alcohol	1: 1,333	53 "	"
	"	1: 1,333	45 "	"
	Pituitary Extract	1:300,000	92 "	"
3E*	Alcohol	1: 1,333	19 m.m.	contraction
	F. E. Cotton R. B. (N. F.)	1: 1,000	38 "	"
	Alcohol	1: 1,333	20 "	"
	F. E. Cotton R. B. (N. F.)	1: 1,000	48 "	"
	Alcohol	1: 1,000	22 "	"
4	Pituitary Extract	1:250,000	27 mm.	contraction
	Alcohol-glycerine, 3-1	1: 100	Relaxation (slight)	
	"	1: 1,000	No noticeable effect	
	F. E. Cotton R. B. (N. F.)	1: 1,000	" "	"
	F. E. Ergot	1: 5,000	5 mm.	contraction
5	Pituitary Extract	1:300,000	26 mm.	contraction
	Alcohol-glycerin, 3-1	1: 1,000	No noticeable effect	
	F. E. Cotton R. B. (N. F.)	1: 1,000	2 mm.	contraction
	F. E. Ergot	1: 5,000	4 "	"
	F. E. Cotton R. B. (N. F.)	1: 1,000	No noticeable effect	
	F. E. Ergot	1: 5,000	3.5 mm.	contraction
6D	Pituitary Extract	1:250,000	24 mm.	contraction
	"	1:250,000	21 "	"
	F. E. Cotton R. B. (N. F.)	1: 1,000	1.5 "	"
	F. E. Ergot	1: 4,000	24 "	"
7C	Pituitary Extract	1:250,000	87 mm.	contraction
	F. E. Cotton R. B. (N. F.)	1: 1,000	14 "	"
	F. E. Ergot	1: 10,000	70 "	"
8B	Pituitary Extract	1:200,000	33 mm.	contraction
	F. E. Cotton R. B. (N. F.)	1: 500	9 "	"
	F. E. Ergot	1: 5,000	24 "	"
9	Pituitary Extract	1:300,000	107 mm.	contraction
	F. E. Cotton R. B. (N. F.)	1: 500	55 "	"
10G	F. E. Ergot	1: 10,000	48 mm.	contraction
	F. E. Cotton R. B. (N. F.)	1: 1,000	26 "	"
	F. E. Ergot	1: 10,000	43 "	"
11	Pituitary Extract	1:300,000	122 mm.	contraction
	F. E. Cotton R. B. (N. F.)	1: 133	115 "	"
	Pituitary Extract	1:300,000	123 "	"
12F	Pituitary Extract	1:250,000	30 mm.	contraction
	F. E. Cotton R. B. (N. F.)	1: 1,000	6 "	"
	Pituitary Extract	1:250,000	11 "	"
	F. E. Ergot	1: 10,000	21 "	"
	Pituitary Extract	1:250,000	73 "	"
	F. E. Cotton R. B. (N. F.)	1: 1,000	6 "	"
	"	1: 1,000	4 "	"
	F. E. Ergot	1: 10,000	5 "	"
	"	1: 10,000	5 "	"
	"	1: 10,000	10 "	"
	"	1: 10,000	31 "	"
	F. E. Cotton R. B. (N. F.)	1: 1,000	22 "	"

Table 7  
ISOLATED UTERUS EXPERIMENTS  
Guinea Pig's Uterus  
Commercial Drug

Experi- ment or Kymo.	Drug	Dilution	Effect	(Contractions, etc.)
13	Pituitary Extract	1:300,000	52 mm.	contraction
	Alcohol	1: 1,333	16 "	"
	"	1: 1,000	13 "	" †H.T.
	"	1: 1,333	10 "	" H.T.
	Pituitary Extract	1:300,000	42 "	" H.T.
	F. E. Cotton R. B. (N. F.)	1: 1,000	14 "	" L.T.
	"	1: 1,000	13 "	" L.T.
	"	1: 1,000	4 "	" L.T.
	Pituitary Extract	1:300,000	6 "	" L.T.
	"	1:300,000	7 "	" L.T.

†H. T. = Higher Tonus. L. T. = Lower Tonus.

14	Pituitary Extract	1:250,000	14 mm.	contraction
	"	1:250,000	13.5 "	"
	Alcohol	1: 1,333	0 "	"
	"	1: 1,333	1 "	"
	"	1: 1,333	1 "	"
	"	1: 1,333	1 (?) "	"
	Pituitary Extract	1:250,000	30 "	"
	"	1:240,000	32 "	"
	F. E. Cotton R. B. (N. F.)	1: 1,000	5 "	"
	"	1: 1,000	4 "	"
	"	1: 1,000	2 "	"
	Pituitary Extract	1:250,000	2.5 "	"
	"	1:250,000	4.5 "	"
15A	Pituitary Extract	1:250,000	65 mm.	contraction
	"	1:250,000	66 "	"
	F. E. Cotton R. B. (N. F.)	1: 1,000	9 "	"
	Pituitary Extract	1:300,000	42.4 "	"
	F. E. Ergot	1: 5,000	70 "	"
	"	1: 10,000	64 "	"
	F. E. Cotton R. B. (N. F.)	1: 1,000	62 "	"
	"	1: 1,000	40 "	"
	"	1: 1,000	10 "	"
	F. E. Ergot	1: 10,000	17.5 "	"
	"	1: 10,000	38.5 "	"
	F. E. Cotton R. B. (N. F.)	1: 1,000	30 "	"

\*The letters indicate the corresponding kymograms on Chart 2.

Power and Browning, cotton root bark contains no tannin.<sup>3</sup> The effect of the alcohol, however, was studied by applying percentages equal to and greater than that found in the solutions of cotton root bark.

Table 7 shows the results of fifteen experiments on the isolated guinea pig's uterus.



Table 8 INTACT UTERUS EXPERIMENTS—CATS

Kymogram 904. Cat Weight 2.38 Kg. Acetoform anaesthesia.	
.5 c.c. per animal F. E. Cotton R. B.	= No contraction.
.5 c.c. " " F. E. Ergot	= Marked contraction.
.5 c.c. " " F. E. Cotton R. B.	= No contraction.
Kymogram 905. Cat Weight 2.3 Kg. Acetoform anaesthesia.	
.2 c.c. per Kg. F. E. Cotton R. B.	= Decided increase in tonus.
.2 c.c. " " "	= Slight " " "
.2 c.c. " " "	= Hardly noticeable effect.
.2 c.c. " " F. E. Ergot	= Slight increase in tonus.
.2 c.c. " " "	= " " "
.2 c.c. " " F. E. Cotton R. B.	= Very slight increase in tonus.
.2 c.c. " " F. E. Ergot	= Slight increase in tonus.
.2 c.c. " " Alc.-glyc. (3-1)	= No effect.
.4 c.c. " " Pituitary Ext.	= Slight increase in tonus.
Kymogram 903. Cat Weight 2.8 Kg. Morph. S.-acetoform anaesthesia.	
.5 c.c. per animal F. E. Ergot	= No contraction.
.005 g. Ergotoxine Phosphate	= Increased tonus.
1 c.c. Pituitary Extract	= " "
1 c.c. F. E. Cotton R. B.	= No effects.
Kymogram 909. Cat Weight 3.05 Kg. Morph. S.-acetoform anaesthesia.	
.5 c.c. per animal F. E. Ergot	= No contraction of uterus.
.5 c.c. " " "	= Distinct contraction.
.5 c.c. " " "	(While uterus was slightly contracted.)
	= Relaxation and then contraction.
.5 c.c. " " F. E. C. R. B.	= Relaxation.
.2 c.c. " " Pituitary Ext.	= Distinct contraction.
Kymogram 907. Cat Weight 2.6 Kg. Morph. S.-acetoform anaesthesia.	
.5 c.c. per animal F. E. Ergot	= Marked contraction of uterus.
.5 c.c. " " F. E. C. R. B.	= " " " "
.5 c.c. " " "	= " " " "
.5 c.c. " " "	= " " " "

Table 9 INTACT UTERUS EXPERIMENTS—RABBITS

Kymogram M-3987-A. Weight of rabbit 2.2 Kg. Pregnant. Paraldehyde.	
.2 c.c. p. Kg. F. E. C. R. B. (50% Alc.)	35 mm. contraction of uterus.
.2 c.c. p. Kg. F. E. C. R. B. (75% Alc.)	28 mm. " " "
.05 c.c. p. Kg. F. E. Ergot (50% Alc.)	50 mm. " " "
Kymogram 3987. Weight 2 Kg. Non-pregnant, multiparous. Paraldehyde.	
.2 c.c. p. Kg. F. E. C. R. B. (50% Alc.)	No effect.
.4 c.c. p. Kg. F. E. C. R. B. (75% Alc.)	No effect.
.1 c.c. p. Kg. F. E. Ergot (50% Alc.)	4 mm. contraction.
Kymogram 3989. Weight 2.2 Kg. Non-preganant, multiparous. Paraldehyde.	
.4 c.c. p. Kg. F. E. C. R. B. (75% Alc.)	12 mm. contraction.
.2 c.c. p. Kg. F. E. Ergot (50% Alc.)	11 mm. " "
.2 c.c. p. Kg. 1:1,000 Pituitary Ext.	12 mm. " "
Kymogram 3990. Weight 2.3 Kg. Non-pregnant, multiparous. Paraldehyde.	
.4 c.c. p. Kg. F. E. C. R. B. (75% Alc.)	No effect.
.2 c.c. p. Kg. F. E. Ergot (50% Alc.)	7 mm. contraction.
Kymogram 4204. Weight 1.56 Kg. Virgin. Paraldehyde.	
.2 c.c. p. Kg. F. E. Ergot (50% Alc.)	Many contr's. One = 47 mm.
.4 c.c. p. Kg. F. E. C. R. B. (75% Alc.)	Wave-like contr's. One = 2.5 mm.
.8 c.c. p. Kg. " " "	" " " One = 1 mm.
.2 c.c. p. Kg. F. E. Ergot (50% Alc.)	Series of contr's. One = 37.5 mm.
Kymogram 4205. Weight 1.66 Kg. Virgin. Paraldehyde.	
.4 c.c. p. Kg. F. E. C. R. B. (75% Alc.)	Tone increased 11 mm.
	Increased contractions.
.6 c.c. p. Kg. " " "	Wave-like contractions = 5 mm.
.2 c.c. p. Kg. F. E. Ergot (50% Alc.)	Series of contr's. One = 18.5 mm.
.1 c.c. p. Kg. " " "	" " " One = 23.5 mm.

## INTACT UTERUS EXPERIMENTS.

The intact uterus experiments were carried out on both cats and rabbits. Nothing was known regarding the previous condition of the cats. For the experiments, they were anaesthetized with acetoform. The rabbits were anaesthetized with paraldehyde. Those which had had young, had previously been used for certain biological tests. The virgins were young animals which were raised at the laboratory. Tables 8 and 9 give the results recorded in these experiments.

## SUMMARY AND CONCLUSIONS.

*Cock's Comb Method.*—Cotton root bark in large doses produced very slight bluing of the cock's comb in a few cases. Doses of the fluidextract fully four times as large as those required of fluidextract of ergot to produce a distinct bluing, failed to produce a comparable effect. Other systemic effects such as dyspnoea and diarrhoea were very pronounced. Owing to these severe symptoms produced by the cotton root bark in the necessarily large doses, and to the unsatisfactory effect on the comb, a close comparison could not be drawn between the activity of this drug and ergot.

By this method, no decided difference could be detected between any of the samples tested, which included root bark from thirteen different varieties of the cotton plant collected at flowering, and several samples of commercial drug both "green" and "dried."

*Blood Pressure Method.*—Cotton root bark produced a slight but transient pressor effect on the blood pressure of the dog. The extent of the effect and the duration were not comparable to that produced by very much smaller doses of ergot. The effect of the cotton root bark usually passed off in 5 or 10 minutes, and occasionally this period was followed by one of lowered pressure. Succeeding doses produced less and less effect. Similarly, ergot following one or more doses of cotton root bark, even though the pressure had not been more than slightly elevated, seemingly did not cause its usual effect.

Five kymograms taken on the intact cat showed either a fall or no effect on the pressure.

On the cat spinal preparation, cotton root bark caused a fall in pressure. One record on a dog spinal preparation showed a slight but very brief rise followed by a fall below normal.

On these preparations, ergot produced a fairly well maintained rise.

By this method, no appreciable or striking difference was noticeable between any of the cotton root products tested.

*Isolated Uterus Method.*—Fluidextract of cotton root bark in rather large doses produced contractions of the isolated, guinea pig uterus. A very conservative interpretation of the results obtained would seem to be that cotton root bark possesses decidedly less than  $\frac{1}{10}$  as much activity as ergot, and decidedly less than  $\frac{1}{30}$  as much activity as commercial pituitary extract. In fact, when given in doses corresponding to these figures, the contractions produced by the cotton root bark were not comparable to those produced by the other substances. Successive doses of cotton root bark produced smaller and smaller contractions. Similarly, ergot and pituitary extract seemingly did not exert their usual effect after one or more doses of cotton root bark. The opposite effect was often observed when any of the three substances was given after ergot or pituitary extract.

By this method, only commercial samples of cotton root bark were tested. No decided difference could be noted between any of these from the results obtained.

Alcohol in a dilution of 1 : 1333, approximately the percentage possessed by a 1 : 1000 dilution of fluidextract of cotton root bark which in several instances was found to be active, caused contractions of the isolated uterus. A 1 : 100 dilution of alcohol caused, in one instance, an inhibition.

*Intact Uterus Method.*—The results obtained on the intact uterus show that cotton root bark possesses a slight action on the uterus of both the cat and the rabbit. The results on the virgin rabbit's uterus were the most satisfactory. These results indicate that the action of cotton root bark is not comparable to that possessed by ergot. As under the other methods, successive doses of cotton root bark seem to produce less and less effect, and ergot given after cotton root bark seems to produce less than its usual effect.

By this method only commercial samples of cotton root bark were tested. No decided difference could be noted between any of these from the results obtained.

#### RECAPITULATION.

Samples of the root bark from thirteen different varieties of the cotton plant, collected at flowering, and a number of samples of commercial root bark, both "green" and "dried," were tested for activity by methods commonly employed for the assay of ergot, namely, the cock's comb, blood pressure, and uterus methods.

Large doses produced a very slight bluing of the cock's comb in

a few cases. In general the results by this method were rather indefinite and unsatisfactory, and no decided difference could be detected between any of the samples tested.

A very slight and transient pressor effect was produced on the blood pressure of the dog. On the intact cat a depressor effect or no effect at all was observed. On the cat spinal preparation a depressor effect was observed, and on a dog spinal preparation a pressor followed by depressor. By this method no decided difference could be noticed between any of the samples tested.

Rather large doses produced small contractions of the isolated guinea pig uterus and the uterus of the cat and rabbit in situ. By the uterus methods only samples of commercial drug were tested. No decided difference could be noticed between any of these from the results obtained.

By the four methods employed, the activity shown by cotton root bark was not comparable to that possessed by ergot.

Tables of results and charts of tracings are given.

I wish to express my obligations to Dr. A. L. Walters under whose supervision this work was carried out.

Credit is due Mr. C. E. Lawson, for preparing the thirteen experimental samples, and Mr. C. C. Hargreaves and Mr. E. E. Swanson for assistance in carrying out the experiments.

#### REFERENCES.

<sup>1</sup> Scott, *Therapeutic Gazette*, 35: 162, 1911.

<sup>2</sup> Sherrington, *Journal Physiology*, 38: 375.

<sup>3</sup> Power and Browning, *Pharmaceutical Journal*, 93: 420-423.

RESEARCH DEPARTMENT,  
ELI LILLY & COMPANY,  
INDIANAPOLIS, INDIANA.

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### THE MACHINERY FOR THE U. S. P. IX REVISION.\*

BY E. FULLERTON COOK, PH.M.

PHILADELPHIA, PA.

#### GENERAL COMMITTEE OF REVISION.

The General Committee of Revision, consisting of 51 members, one of whom was the President of the Convention, ex-officio, having been elected by the Pharmacopœial Convention of 1910, the com-

\* Read before the Philadelphia Branch of the American Chemical Association.

mittee proceeded to elect its chairman, but largely left in his hands the details of organization.

There was to be an Executive Committee of fifteen members to be elected from the General Committee and presided over by the chairman of the General Committee, and it was understood that there would be sub-committees.

Professor Remington, the elected chairman, fortunately had experience in revision work covering at least four decades, and qualified by his natural organizing ability, was able to create a machine which worked harmoniously and effectively. With the approval of the Committee and Board, the following general plan of organization was carried out:

*Sub-Committee.*—Each member of the General Committee was invited to express his preference for the type of revision work which he would care to assume, the list of sub-committees having been decided upon at the first meeting of the committee in Washington. These sub-divisions consisted of:

- 1 Scope.
- 2 Therapeutics, Pharmacodynamics and Posology.
- 3 Biological Products, Diagnostical Tests.
- 4 Botany and Pharmacognosy.
- 5 General and Inorganic Chemistry.
- 6 Organic Chemistry.
- 7 Proximate Assays.
- 8 Volatile Oils.
- 9 Fluid and Solid Extracts, Tinctures.
- 10 Aromatic Waters, Spirits, Liquors.
- 11 Syrups and Elixirs.
- 12 Cerates and Ointments.
- 13 Miscellaneous Galenicals.
- 14 Tables, Weights, Measures.
- 15 Nomenclature.

From these preferences, the chairman of the General Committee appointed sub-committee members. Naturally, the botanists indicated their preference for that type of work; chemists selected chemical subjects; the physicians, scope, therapeutics and related subjects; while the pharmacists were especially interested in pharmaceutical preparations. These assignments by one who was personally acquainted with practically every member of the committee, proved

generally acceptable and satisfactory. The appointments, however, according to the by-laws, were confirmed by the General Committee and Board of Trustees. Each sub-committee then proceeded to elect its chairman, the election being finally approved by the General Committee and Board of Trustees.

*Executive Committee.*—By common consent, it was then decided that the chairman of sub-committees would constitute the Executive Committee, the general chairman presiding according to the by-laws. This plan has been very effective, as the Executive Committee has thus consisted of representatives from every sub-committee and naturally, being chairman, they were all active workers.

*Method of Revision.*—The following plan of procedure was then adopted: The Sub-committee on Scope decided very promptly upon the majority of the substances to enter the new Pharmacopœia. This list, over which there was no difference of opinion, was immediately placed in the hands of the other sub-committees for their consideration, while the Sub-committee on Scope proceeded with the further consideration of drugs, chemicals and preparations, over which there was some question concerning admission. As these were decided they were reported to the Executive Committee, with the vote in the Sub-committee on Scope and finally, if admitted, referred to the proper Sub-committee for revision. As a preparation, drug or chemical, or possibly a process, was referred to a sub-committee, the chairman was given entire liberty of action and two different methods were in general use, depending upon the preference of the presiding officer. In one instance, the chairman compiled all available data on each subject, and submitted it to his sub-committee for their consideration and comment. Having completed this step, and any necessary experiments or tests, he then prepared a tentative text, embodying the desired changes, as indicated by his own experience and experiments, and the recommendations of members of his sub-committee. The text was then submitted to the sub-committee and again subject to their criticism. When finally satisfactory to the sub-committee, the revised text was sent to the chairman of the Executive Committee who modified the wording, if necessary, to bring it into harmony with the editorial style decided for the new book, and then submitted it to the Executive Committee for their comment.

The other plan used by some sub-committee chairmen was to

assign the subjects submitted for revision, to individual members and ask that reports be made promptly to the chairman of the sub-committee, embodying the proposals for a revised text. These reports were in turn submitted to the entire sub-committee by the sub-committee chairman and when finally approved, placed before the Executive Committee. The general chairman now compiled all comments and discussions, submitted by the members of the Executive Committee and these were published before the entire Executive Committee, and copies sent to the members of the sub-committee which had submitted the original report.

When practically all of the articles submitted to a sub-committee had been reported upon, in most instances arrangements were made for the members of the sub-committee to hold a personal conference, when all suggestions or adverse criticisms were considered, and a report drawn up for submission to the General Committee. At this time, the chairman of the General Committee again carefully revised the copy from an editorial standpoint, and submitted it in full, as proposed for inclusion in the new Pharmacopœia, to all members of the General Committee.

It must not be thought that the General Committee had no part in the revision up to this time. Many subjects of general interest, and policies and principles of the revision had been placed before the General Committee and the work proceeded, all comments received from many sources and as submitted to the convention, had been published in the general committee circulars. Another feature, which proved of great value was the placing of monthly "reports on progress" from every sub-committee, before the General Committee. This feature of the revision work was not generally known, but the general chairman sent a request to every sub-committee chairman, about ten days before the end of each month, asking him to fill out an enclosed blank. This blank covered all likely activities of the sub-committee during the month, and these were compiled and submitted regularly to the General Committee as already indicated. This plan increased activity in the sub-committees and at the same time kept the General Committee familiar with all parts of the work. As the revision work is largely voluntary, it was found desirable to use this publicity method, within the committee, to stimulate progress.

At the same time that this material was submitted to the General Committee, abstracts of proposed changes were prepared and pub-

lished in the *Journal of the American Pharmaceutical Association*, and reprints very generally distributed, so that the country could see what changes were proposed in advance of the actual publication of the book. In the experience of the last committee, it was shown that any extensive publicity of proposed changes prior to this point, would be premature. During the actual discussion on revision, the work would be prolonged beyond all reasonable time if the public were admitted to the preliminary committee conferences, and discussions are more free and valuable if kept within the sub-committees. The experience of the last Revision Committee has shown that publication at this stage of the revision gives ample time for those who are not on the committee to give valuable criticism or recommendations and this feature should remain a part of any revision scheme.

*Preparing the Manuscript.*—Ample time having been allowed for comments from the committee and also from those who were interested in Pharmacopœial revision, who were not members of the committee, but had access to the public abstracts, these were assembled on sheets containing the latest copy of the proposed text, as submitted to the General Committee, and were given detailed consideration by the chairman, in conference with the different sub-committee chairmen. Those which were found of vital importance and sufficiently tested, were embodied in the text. The manuscript was now made up—every title, the construction of sentences, capitalization, punctuation, and other editorial detail being given a final polishing, and the manuscript sent to the printer.

Of course, before this time, sample pages to show styles of type and general arrangement, had been approved. The galley proofs were submitted on standard size paper ( $8\frac{1}{2} \times 11$ ) perforated for binding, and were clean impressions taken from a press, so that they were perfectly legible. The galley was now sent to every member of the Executive Committee, in duplicate, and as the galleys were returned by the members to the general chairman, the comments were assembled in the chairman's office upon one set of galleys. These comments were once more given consideration in conference with the sub-committee chairman, and corrected copy for page proof returned to the printer. Page proof in duplicate was now submitted to every member of the General Committee, and the returned comments from the General Committee once more assembled



on one set of page proof, and from this material the copy for foundry proof was prepared. The general chairman finally passed upon the foundry and plate proofs and printing was ordered. Two thousand copies were in the first printing, and these were sent to the journals for review, to all members of the Committee of Revision, and a few were sold. A few typographical errors were discovered by this critical review of the finished book and these were all corrected in the plates before the first large edition of 10,000 copies was printed, so that the main edition, from the very start of the printing, was free from the majority of the errors which have been only recently announced.

As a result of the experience in the revision of the U. S. P. IX there is one outstanding feature which would seem to lend itself to broader application in the next revision, namely, an increased number of personal conferences. While it is true that the next revision of the Pharmacopœia does not seem to call for as extensive alteration, in either style or fact, as heretofore, and therefore will naturally require much less time for revision than the U. S. P. IX, yet the correspondence method is so cumbersome and time-consuming, that the conference plan for getting results would greatly lessen the necessary time of revision. As an illustration of the time necessary for the correspondence method, with the committee scattered over a large part of the United States, and the time for an exchange of mail being at least five days in some instances, the following general plan had to be followed in voting:

The subject for consideration was presented to the committee by the general chairman, with a statement of the proposal and any necessary explanations or comments for the members. Two weeks was allowed for assembling all discussions. At the end of two weeks, a voting sheet was mailed to each member with all the comments on the proposition. Two weeks was again allowed for the return of the voting sheets before the result of the vote was announced, thus four weeks was the minimum time required for a vote. As frequently happened, a member would submit an amendment, which required another two or four weeks for final settlement. Thus it will be seen that the hundreds of problems before the committee involve an extended time for final agreement.

It is therefore suggested that when the General Committee of Revision of the U. S. P. IX submits its recommendations to the convention for procedure in the new revision, that they advise the new

General Committee to meet for at least one day following the convention, elect a chairman, sub-committees, and sub-committee chairmen and dispose of a few of the more important questions of policy before adjourning.

There should then be arranged a personal conference for each sub-committee as soon as they have enough material before them for arriving at decisions which would probably be about six months after their organization. The most important modification to increase efficiency and lessen the time of revision, however, would be a personal conference of the Executive Committee, at least once in each two months during the active work of revision. In the interim, the general chairman could place many problems before the committee, with discussions, and a program for a conference at an agreed time, when most of the questions under consideration could be decided in a one-day meeting. Full stenographic details of the conferences should be presented to each member immediately after the meeting and the decks being cleared by the conference, new work could be considered in preparation for the next meeting. It is believed that if the Executive Committee again consists of the sub-committee chairmen, that these personal conferences will tremendously stimulate the work of the sub-committees, as each chairman will be expected to report in full the condition of his own sub-committee at each of these conferences. This of course, will necessitate a personal sacrifice of the time on the part of the members of the Executive Committee, but it is believed that this method will so greatly facilitate the work of revision, that it can be concentrated into the first year and everyone promptly relieved of the burden. Of course, railroad and hotel expenses of these conferences should be met by the convention.

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### CAFFEINE FROM COFFEE SOOT.\*

SUGGESTION FOR RECLAIMING A PORTION OF THE CONSTITUENTS WHICH ARE  
VOLATILIZED IN THE ROASTING PROCESS.

BY GEORGE E. ÉWE.

PHILADELPHIA, PA.

The soot which collects in the flues and on the upper inner surface of coffee roasters frequently contains enough caffeine to warrant its use as a raw material for the production of this valuable sub-

\* From *The Tea and Coffee Trade Journal*, March, 1920.

stance. Since there is considerable demand for caffeine, the collection of coffee soot, if established upon a profitable basis, would result in an added source of income to coffee roasting firms.

In order to interest roasters in the collection of the "soot," a statement regarding the probable price which might be obtained for it is pertinent. No market price has been thoroughly established for this article, because it varies greatly in caffeine content. Specimens recently examined in the Pharmaceutical Research Laboratories of the H. K. Mulford Co., Philadelphia, ranged all the way from 0.08 to 22.2 per cent. in caffeine content.

SOME ANALYSES OF COFFEE SOOT.

Sample No.	Caffeine Content.	Source of Sample. <sup>1</sup>
1.....	22.20%	Flue of roaster.
2.....	18.30%	Flue of roaster.
3.....	11.94%	Inner walls of roaster.
4.....	3.25%	Ceiling of roaster.
5.....	1.76%	Dust collector on roof (mixed with chaff).
6.....	0.70%	Flue of roaster.
7.....	4.18%	Flue of roaster.
8.....	1.20%	Flue of roaster.
9.....	7.10%	Flue of roaster.
10.....	11.20%	Flue of roaster.
12.....	0.08%	Flue of roaster.
13.....	4.42%	Ceiling of roasting room.
14.....	15.30%	Flue of roaster.

Since tea fluff, tea siftings, and damaged tea, which contain from 1 to 5 per cent. of caffeine, are commonly used raw materials for the production of caffeine, it is evident that collections of coffee soot with similar caffeine contents would be excellent material for the production of caffeine and should command a price approximately equal to that of these tea materials. These tea materials were quoted around 10c. per lb. during December, 1919. It is encouraging to report here that one-half of the coffee soot samples which we have examined, possessed caffeine contents which were well above the maximum content of the starting materials obtained from tea.

A statement regarding the probable amount of soot collectable from roasters in a given time would also be pertinent, but un-

<sup>1</sup> None of the commercial roasters from which these samples were obtained, were equipped with collectors for the express purpose of collecting the "soot," and only one (No. 5) was equipped with a dust collector.

fortunately this cannot be offered, for the reason that no commercial roaster equipped with a soot collector was met with in this investigation. Only a properly designed and properly operated soot collector will yield figures for this.

By coffee soot is meant the smoke-like vapor which arises from the roasting barrel during the roasting process. Coffee chaff, which is also a by-product of the roasting of coffee, also contains caffeine, but its economic use for the production of caffeine has not been rendered possible up to the present time. It contains much smaller proportions of caffeine than the raw materials from tea, and in addition contains considerable pyroligneous or tarry matter which makes the production of pure white caffeine very difficult and expensive. Specimens of coffee chaff recently examined in the Mulford laboratories ranged between 0.6 and 1.1 per cent. in caffeine content.

#### METHODS OF COLLECTING COFFEE SOOT.

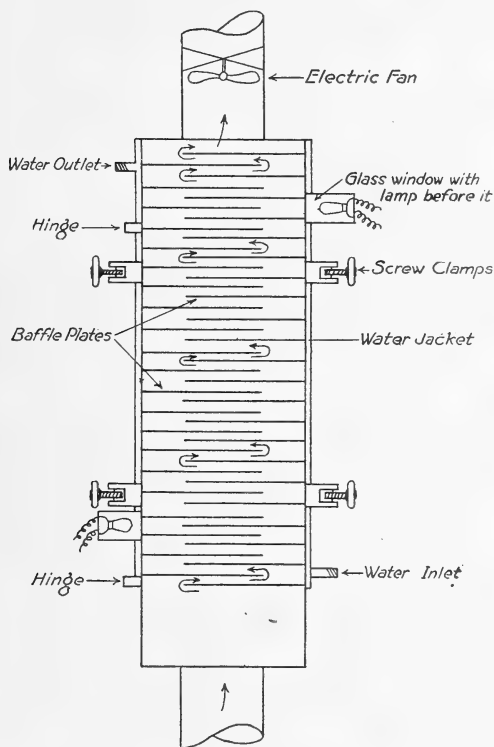
Caffeine is a sublimable substance, that is, it can be made to pass into the form of a vapor by heat; and upon cooling this vapor, the caffeine will be precipitated as a crystalline "snow." It is by the principle of sublimation that caffeine is collected; since the utilizable constituent of coffee soot and flue gases from the roasting of coffee is caffeine, it is by sublimation that the caffeine containing coffee soot is best collected.

Coffee soot escapes from the roaster *via* the flue. In practice, a considerable proportion also escapes into the room in which the roaster is situated, and where the collection of the soot is made a practice for profit, it is a source of loss of income. This loss can be prevented by proper regulation of the draft in the flue as described later in this article. Since coffee soot escapes *via* the flue, it is necessary, therefore, to connect the collector with the flue. Theoretically, the conditions required are a means of cooling the coffee soot and flue gases to precipitate the caffeine contained in them; a collector to retain the precipitated caffeine and soot; and a draught regulator to control the rate of flow of the soot and gases through the collector so that it is not so fast that caffeine passes through the collector and is lost in the outer air, nor so slow that the soot is lost by being forced out into the air of the room in which the roaster is situated.

The illustration herewith shows the details of a practical coffee soot collector.

DETAILS OF A COFFEE-SOOT COLLECTOR.

The collector consists of a water-jacketed, sheet-iron or cast-iron box equipped with baffle plates arranged so as to make a tortuous



*FRONT VIEW (without door)*

*Cross-section of a Coffee Soot Collector.*

path for the soot from the coffee-roaster. It is connected in an upright position with the flue of the roaster.

If the resistance of the baffle plates is too great to permit the passage of the soot and flue gases, an electric fan must be installed in the exit pipe of the collector. The suction thus created must be just enough to prevent the soot and gases from coming out into the room in which the roaster is situated, and not enough to carry any of the chaff up into the collector.

The water jacket is required to be operated only in the summer, and may not be necessary at all in connection with smaller roasters.

The glass windows with incandescent lamps before them, in the sides of the collector, are required during the installation of the collector when the best conditions for operation are being established.

The door of the collector is attached very loosely so as to allow a final tight adjustment by means of the four screw clamps. A soot-tight joint is obtained by means of an asbestos or composition gasket fixed in a slot around the inner edge of the door.

The interior of the collector is painted with aluminum paint, to prevent rust from forming and becoming mixed with the soot.

The collected soot is removed by releasing the screw clamps, throwing back the door on its hinges and scraping out the soot with a long steel or wooden blade.

Only the soot, and not the chaff, possesses any degree of commercial value, therefore the collector will probably not be applicable to the collection of soot from the type of roaster in the flue of which a strong blower must be employed, for the reason that the chaff and soot are usually inseparably mixed by the blower. The collector can be applied to the collection of soot from a roaster equipped with a blower by reducing the speed of the blower, so that none of the chaff is blown up into the collector, the speed of the blower being only enough to prevent the escape of soot and flue gases into the room in which the roaster is situated. If the purpose of the blower is the removal of the chaff, reduction of its speed to collect the soot will nullify this purpose and add an operation to the roasting process, namely the removal of the chaff. This will increase the expense of coffee-roasting process, and should be debited against the returns to be expected from the collection of the soot.

#### FOR EITHER GAS OR COAL ROASTERS.

The collector is applicable to the collection of coffee soot from either gas-fired or coal-fired roasters, but it must be remembered that coal soot or gas soot have no value, and therefore efforts must not be directed toward the production of these types of soot.

No dimensions are indicated in the drawing of the collector, as any size can be used according to requirements; merely keeping the dimensions in approximately the same ratio as they appear

in the drawing. For a single roaster, it is likely that a collector 6 feet in height will completely collect the soot.

To the writer's knowledge the collection of coffee soot is not being practiced in this country, but is in Continental European countries with reputed satisfactory returns. The Continental preference for more thoroughly roasted coffee may be a factor in this respect, because the soot would consequently be richer in caffeine. Whether coffee soot can be established as a profitable source of caffeine in this country is problematical and is a challenge to our best efforts.

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## THE STRUCTURE OF ATOMS AND ITS BEARING ON CHEMICAL VALENCE.\*

BY IRVING LANGMUIR,

GENERAL ELECTRIC CO., SCHENECTADY, N. Y.

According to the well-established Rutherford-Bohr theory, all the positive electricity in an atom is concentrated in a *nucleus* at its center. The dimensions of this nucleus are negligibly small compared with those of the rest of the atom, its diameter being of the order of 0.00001 of that of the atom. The charge on the nucleus is an integral multiple of the charge of an electron but, of course, opposite in sign. The remainder of the atom consists of electrons arranged in space about the nucleus, the normal number of such electrons (called the *atomic number*) being equal to the number of unit positive charges on the nucleus, so that the atom as a whole is electrically neutral. If the number of electrons in the atom exceeds the atomic number we have a negatively charged atom or ion, while in the reverse case a positively charged atom or ion results. The atomic number of any element has been found to be equal to the ordinal number of the element in the periodic table. Thus hydrogen has the atomic number 1, helium 2, lithium 3, carbon 6, neon 10, chlorine 17, nickel 28, silver 47, cerium 58, tungsten 74, radium 88, and uranium 92. The atomic numbers can be determined experimentally from the X-ray spectrum so that we are not dependent upon the periodic table for our knowledge of these numbers.

\* From *The Jour. of Indus. and Engineering Chem.*, April, 1920.

Bohr, Sommerfeld, and others have developed an extensive and very successful theory of spectra upon the hypothesis that the electrons in atoms are in rapid rotation in plane orbits about the nucleus in much the same way as the planets revolve around the sun. Stark, Parson, and G. N. Lewis, on the other hand, starting from chemical evidence, have assumed that the electrons are stationary in position. It should be noted that Bohr's theory has had its greatest success when applied to atoms or ions containing only one electron and that it seems incapable of explaining the chemical or ordinary physical properties of even such simple elements as lithium, carbon, or neon.

The two theories can, however, be reconciled if we consider that the electrons, as a result of forces which they exert on one another, rotate about certain definite positions in the atom which are distributed symmetrically in three dimensions. Thus for atoms containing only a single electron the chemical theory is in agreement with Bohr's theory. But for an atom such as neon the eight electrons in the outside layer would revolve around positions which are located about the nucleus in the same way that the eight corners of a cube are arranged about the center of the cube. This structure is not inconsistent with those parts of Bohr's theory which have received experimental confirmation. In fact, Born and Landé,<sup>1</sup> starting with Bohr's theory and without knowledge of Lewis' work, arrived at exactly this conception of the structure of atoms (*i. e.*, the cubic atom) from a study of the compressibility of the salts of the alkali metals.

The atomic numbers and the properties of the inert gases furnish us with a clue to the arrangement of the electrons within atoms. The low boiling point, the high ionizing potential, the chemical inertness, etc., of helium prove that the arrangement of the electrons in the helium atom is more stable than that in any other atom. Since this atom contains two electrons we must conclude that a pair of electrons in the presence of a nucleus represents a very stable group. It is reasonable that with elements of higher atomic numbers there should be an even greater tendency for this stable pair of electrons to form about the nucleus. There are two sets of facts which furnish conclusive experimental evidence that this stable pair exists in all atoms above helium.

<sup>1</sup> *Verh. d. phys. Ges.*, 20: 210, 1918.



In the first place; the properties of lithium, beryllium, etc., show that in these elements also the first two electrons are held firmly while the remainder are easily detached. Thus, lithium readily forms a univalent positive ion by the detachment of one of the three electrons in its neutral atom. The divalence and other properties of beryllium prove that there is little or no tendency for a second stable pair of electrons to surround the first pair.

In the second place, the absence of irregularities in the observed K and L series of the X-ray spectra of the various elements proves that there are no sudden changes in the number of electrons in the innermost layers of electrons about the nucleus. From these two sets of facts, as well as from other evidence, we may take it as a fundamental principle that the arrangement of the inner electrons undergo no change as we pass from elements of smaller to those of higher atomic number.

The properties of neon indicate that its atoms are more stable than those of any other element except helium. Since the atomic number is 10, and the first 2 electrons form a stable pair about the nucleus as in the helium atom, it follows directly that the other eight electrons arrange themselves in a second layer or shell possessing a very high stability. If these 8 electrons revolved about the nucleus in a single circular orbit or ring, as would be suggested by Bohr's theory, there is no apparent reason why there should be any very great difference in stability between rings having 7, 8 or 9 electrons. On the other hand, we readily see that the geometrical symmetry of the arrangement of the 8 electrons at (or rotating about) the 8 corners of a cube would not only account for a high degree of stability but for the fact that an arrangement of 7 or 9 electrons would have no such stability. Chemical considerations and Born and Landé's work on compressibility also lead us to this spatial arrangement of the electrons. We shall refer to the stable group of 8 electrons by the term *octet*. From the principles already enunciated it is clear that in the atoms of all the elements above neon the inner electrons are arranged in the same way as those of neon.

From the atomic numbers of the inert gases we are thus able to determine the number of electrons in the various layers or shells of electrons which exist in the atoms. The results are summarized in Table 1.

Thus the xenon atom with an atomic number 54 contains 54 electrons arranged as follows: Close to the nucleus are two elec-

TABLE I—DISTRIBUTION OF ELECTRON IN THE VARIOUS SHELLS.

Shell.	Number of Electrons.	Inert Gas Corresponding to Completed Layer.
1st shell.....	$2 = 2 \times 1^2$	He 2
2nd shell, 1st layer.....	$8 = 2 \times 2^2$	Ne 10
2nd shell, 2nd layer.....	$8 = 2 \times 2^2$	Ar 18
3rd shell, 1st layer.....	$18 = 2 \times 3^2$	Kr 36
3rd shell, 2nd layer.....	$18 = 2 \times 3^2$	Xe 54
4th shell, 1st layer.....	$32 = 2 \times 4^2$	Nt 86

trons which constitute the first shell. This is surrounded by the second shell which contains two "layers" of 8 electrons each. The third shell, which in the xenon atom is the outside shell, contains 18 electrons.

An examination of the numbers of electrons in the layers (Table I, 2nd column) shows that they bear a simple mathematical relation to each other, namely, that they are proportional to the squares of the successive integers 1, 2, 3 and 4. This is to be looked upon as perhaps the most fundamental fact underlying the periodic arrangement of the elements. It is significant that in Bohr's theory these same numbers, 1, 4, 9, 16, etc., play a prominent part. Thus the energies of the electron in the various "stationary states" are proportional to 1,  $1/4$ ,  $1/9$ ,  $1/16$ , etc., and the diameters of the various possible orbits in Bohr's theory are proportional to 1, 4, 9, 16, etc. In Bohr's theory the various stationary states correspond to different number of quanta (Planck's quantum theory), the innermost orbit corresponding to one quantum, the second orbit to two quanta, etc. We should thus consider (Table I) that the electrons in the 1st shell are monoquantic, those in both layers of the 2nd shell are diquantic, etc. It is interesting that Born and Landé, from quite other evidence, have concluded that the outermost electrons of the chlorine atom (2nd layer of the 2nd shell) are diquantic instead of triquantic, as was at first assumed.

The foregoing theory of the arrangement of electrons in atoms explains the general features of the entire periodic system of the elements and is particularly successful in accounting for the position and the properties of the so-called 8th group and the rare earth elements. It also serves to correlate the magnetic properties of the elements.

Let us now consider the bearing of this theory of atomic structure on the phenomena of chemical valence. The outstanding fea-

ture of the theory is that there are certain groups of electrons, such as the pair in the first shell and the octet in the second, that have a remarkable stability. Those atoms in which all the electrons form parts of such stable groups (*viz.*, the inert gases) will have no tendency to change the arrangement of their electrons and will thus not undergo chemical change. Suppose, however, we bring together an atom of fluorine ( $N = 9$ )<sup>1</sup> and an atom of sodium ( $N = 11$ ). Ten electrons are needed for the stable pair in the first shell and the octet in the second shell, as in the neon atom. The sodium atom has one more electron than is needed to give this stable structure while the fluorine atom has one electron too few. It is obvious then that the extra electron of the sodium atom should pass over *completely* to the fluorine atom. This leaves the sodium atom with a single positive charge while the fluorine becomes negatively charged. If the two charged atoms or ions<sup>2</sup> were alone in space they would be drawn together by the electrostatic force and would move as a unit and thus constitute a molecule. However, if other sodium and fluorine ions are brought into contact with the "molecule" they will be attracted as well as the first one was. There will result (at not too high temperature) a space lattice consisting of alternate positive and negative ions and the "molecule" of sodium fluoride will have disappeared. Now this is just the structure which we find experimentally for sodium fluoride by Bragg's method of X-ray crystal analysis. There are no bonds linking individual pairs of atoms together. The salt is an electrolytic conductor only in so far as its ions are free to move. In the molten condition or when dissolved in water, therefore, it becomes a good conductor.

The case of magnesium ( $N = 12$ ) and oxygen ( $N = 8$ ) is similar except that two electrons are transferred from the magnesium to the oxygen atom. The resulting ions have their electrons arranged exactly like those of the neon atoms and the ions of sodium

<sup>1</sup> We will denote the atomic number of an element by  $N$ .

<sup>2</sup> It is convenient and it has been customary with many physicists to speak of a charged atom or molecule as an ion, irrespective of whether or not the particle is able to wander under the influence of an electric field. The writer has used the term in this way in his recent publications. This practice is very distasteful to many physical chemists and is apt to be misunderstood by them. Nevertheless, it seems to me probable, especially in view of the recent work of Milner and Ghosh, that it will be desirable to abandon the physical chemists' definition of the ion and to apply it to all charged atoms or molecules. The ion which wanders may then be referred to as a "free ion."

and fluorine. Therefore, the crystalline form of magnesium oxide and sodium fluoride should be identical, and this prediction of the theory has been confirmed experimentally by Dr. A. W. Hull by the X-ray method. Because of the much greater forces acting between the ions as a result of the double charges, the stability of the magnesium oxide is much higher than that of the sodium fluoride. This is manifested by the high melting point, low conductivity, low solubility, and hardness of magnesium oxide.

Phosphorus ( $N = 15$ ) and sulphur ( $N = 16$ ) have, respectively, 5 and 6 electrons more than neon, and are thus capable of giving up these numbers of electrons. If these elements are brought into contact with an excess of fluorine (which because of its proximity to neon has a particularly strong tendency to take electrons) all the extra electrons pass to fluorine atoms. Thus a sulphur atom will supply electrons to 6 fluorine atoms and will form the compound  $SF_6$ . The force acting between the fluorine ions and the central sulphur ion is still electrostatic in nature it must be nearly 6 times greater than the force between sodium and fluorine ions. Furthermore, the 6 fluorine ions would surround the sulphur ion so that there would be little stray field of force. Therefore, we should not expect sulphur fluoride to be salt-like in character but to consist of very stable molecules having weak external fields of force and, therefore, readily existing in the form of a gas. As a matter of fact, this extraordinary substance has these properties developed to such a degree that it is an *odorless* and *tasteless* gas with a boiling point of  $-62$  deg. Phosphorus pentafluoride, as would be expected from its less symmetrical structure, is a gas having greater chemical activity.

The fluosilicate ion  $SiF_6^{--}$  has a structure exactly like that of the sulphur fluoride molecule, since the number and arrangement of the electrons are the same. This is clear if we consider that the atomic number of silicon is 14 while that of sulphur is 16. Thus if we should replace the nucleus of the sulphur atom in a molecule of sulphur fluoride by the nucleus of a silicon atom, without disturbing any of the surrounding electrons, we would have removed two positive charges and would obtain a negative ion with two negative charges of the formula  $SiF_6^{--}$ . In the presence of potassium ions we would then have the familiar salt potassium fluosilicate. The theory is thus capable of explaining typical complex salts. In fact, it is applicable to the whole field of inorganic compounds

covered by the work of Werner, and helps to simplify the theory of such compounds. There is no time, however, to go into this subject.

The simple theory of atomic structure which we have discussed thus far explains perfectly what has usually been called "the maximum positive and negative valence." The maximum positive valence represents the number of electrons which the atom possesses in excess of the number needed to form one of the particularly stable configurations of electrons. On the other hand, the maximum negative valence is the number of electrons which the atom must take up in order to reach one of these stable configurations.

For example, magnesium has a positive valence of two, since its atomic number is 12, while that of neon is 10. Sulphur has a positive valence of 6, since it has 6 electrons more than neon; but it has a negative valence of two because it must take up more electrons before it can assume a form like that of the argon atom.

It is clear, however, that this theory of valence is not yet complete.<sup>1</sup> It is not applicable to those cases where we have usually taken valences of 4 for sulphur, or 3 and 5 for chlorine, etc. But more especially it does not explain the structure of organic compounds and such substances as  $H_2$ ,  $Cl_2$ ,  $O_2$ ,  $N_2H_4$ ,  $PCl_3$ , etc.

J. J. Thomson, Stark, Bohr, and others had suggested that a pair of electrons held in common by two adjacent atoms may function in some cases as chemical bonds between the atoms, but this idea had not been combined with the conception of the stable groups of electrons or octets. G. N. Lewis, in an important paper in 1916, advanced the idea that the stable configurations of electrons in atom could share *pairs* of electrons with each other and he identified these pairs of electrons with the chemical bond of organic chemistry. This work of Lewis has been the basis and the inspiration of my work on valence and atomic structure.

As a result of the sharing of electrons between octets, the number of octets that can be formed from a given number of electrons is increased. For example, two fluorine atoms, each having seven electrons in its outside shell, would not be able to form octets at all except by sharing electrons. By sharing a single pair of electrons, however, two octets holding a pair in common required only 14

<sup>1</sup> The theories of Kossel, Lacomblé, Teudt, etc., which have recently been proposed in Germany, have not advanced beyond this point and are therefore very unsatisfactory as a general theory of valence.

electrons. This is clear if we consider two cubes with electrons at each of the eight corners. When the cubes are placed so that an edge of one is in contact with an edge of the other a single pair of electrons at the ends of the common edge will take the place of four electrons in the original cubes. For each pair of electrons held in common between two octets there is a decrease of two in the total number of electrons needed to form the octets.

Let  $e$  represent the number of electrons in the outside shell of the atoms that combine to form a molecule. Let  $n$  be the number of octets that are formed from these  $e$  electrons, and let  $p$  be the number of pairs of electrons which the octets share with one another. Since every pair of electrons thus shared reduces by two the number of electrons required to form the molecules it follows that  $e = 8n - 2p$  or  $p = \frac{1}{2}(8n - e)$ .

This simple equation tells us in each case how many pairs of electrons or chemical bonds must exist in any given molecule *between the octets formed*. Hydrogen nuclei, however, may attach themselves to pairs of electrons in the octets which are not already shared. For example, in the formation of hydrogen fluoride from a hydrogen atom and a fluorine atom there are 8 electrons in the shells ( $e = 8$ ). We place  $n = 1$  in the above equation and find  $p = 0$ . In other words, the fluorine atoms do not share electrons with each other. The hydrogen nucleus having given up its electron to the fluorine atoms attaches itself to one of the pairs of electrons of the fluorine octet, and thus forms a molecule having a relatively weak external field of force. As a result, hydrogen fluoride is a liquid of low boiling point instead of being salt-like in character.

The equation given above is applicable to all types of compounds. For example, if we apply it to substances such as sodium fluoride, sulphur fluoride, or potassium fluosilicate, which were previously considered, we find in each case  $p = 0$ . In other words, there are no pairs of electrons holding the atoms of these compounds together. On the other hand, if we consider the compound  $N_2H_4$ , we find  $p = 1$ . Since there are only two octets, the pair of electrons must be between the two nitrogen atoms while the hydrogen nuclei attach themselves to pairs of electrons of the nitrogen octet. It can be readily shown that this simple theory is in fact identical with the accepted valence theory of organic chemistry and leads to the same structural formulas as the ordinary theory in all those

cases where we can take the valence of nitrogen to be 3, oxygen and sulphur 2, chlorine and hydrogen 1. In other cases, such as those where quinquivalent nitrogen has been assumed, the new theory gives results different from the old, but in each case in better agreement with the facts.

The theory indicates a series of new relationships between certain types of substances which I have termed *isosteric* substances. For example, it indicates that the molecules of carbon dioxide and nitrous oxide should have nearly identical structures and this is borne out by the extraordinary similarity in the physical properties of these gases. Nitrogen and carbon monoxide constitute another pair of gases which are similarly related. The same theory also points out a number of previously unsuspected cases of similarity of crystalline form (isomorphism).

It is clear that in the past the term valence has been used to cover what we may now recognize as three different types of valence, as follows:

1. Positive valence: the number of electrons an atom can give up.
2. Negative valence: the number of electrons an atom can take up.
3. Covalence: the number of pairs of electrons which an atom can share with its neighbors.

It is recommended that only for valences of the covalence type should definite bonds be indicated in chemical formulas. One of the particular advantages of the present theory is that it becomes easy to distinguish between covalence and the other types and thus to predict with certainty in what way electrolytic dissociation will occur, if at all.

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### WHEN IS POISON NOT A POISON?\*,<sup>1</sup>

BY JOHN URI LLOYD, PHARM. M.,

CINCINNATI, OHIO.

A reply to the above question might be: When, for any reason, a substance is harmless in action, immediate or remote, be it applied

externally or taken internally. In other words, it is *not then a poison*.

This leads to the question: "Can a substance be considered as a poison at one time and innocuous at another?" To this one might make several replies, as the problem is viewed from its several side-angles.

For example, sulphuric acid, in concentrated form, applied to the skin or taken internally, will at once disintegrate flesh. Its action is then that of a corrosive agent, its destructive influence resting directly upon avidity for water and its power of abstracting water from liquids and even from tissue, to the tissue's complete destruction. It thus, under these conditions, becomes a corrosive poison.

As an example, one might state that white sugar is a carbohydrate, composed of carbon and the elements of water in the proportion to theoretically produce water. Place a lump of white sugar on a plate and then pour upon it a little concentrated sulphuric acid. Immediately it turns yellow, then black, owing to the liberation of carbon (charcoal) by the abstraction of its companion oxygen and hydrogen, which the acid takes, to the destruction of the sugar.

Dilute the same amount of sulphuric acid with water, to pleasant acidity, and it no longer destroys tissue on contact therewith, nor is it immediately harmful to the stomach. The sugar dissolves in it, colorless, when it is thus diluted. Indeed, as an acidulated drink (circus lemonade), much diluted and flavored with lemon oil, it has been used, without immediate corrosive effect or injury, as a substitute for lemonade. This practice, however, is now wisely forbidden.

To sum up, in one form, sulphuric acid is destructive to living tissue; in another form (dilute), it acts differently. The amount that, concentrated, would disintegrate tissue if applied locally, is, when diluted, harmless.

Take next arsenic. With the normal human being, arsenic, in comparatively small doses, is death-dealing. But with some persons, artificially made immune, a dose that poisons others is harmless. Arsenic eaters come within the scope of habit-forming drug addicts. The habit-formed principle applies likewise to morphine and similar drugs. Be the arsenic or morphine dilute or concentrated, a toxic amount to the normal man acts as a poison. Be it, for example, six grains of morphine, in substance, or six grains dissolved in an ounce of water, the same exerts its poisonous influence, providing



the whole amount be taken at a single dose. Indeed, dilution may even increase its activity.

Be it said that, although arsenic, morphine and such as these act as poisons upon the normal man, an individual may, as above stated, accustom his system to the drug, so that enormous doses may be taken without apparent injury. In this no comparison can be made with the cited action of sulphuric acid of which a drop on the skin of any man will bite its way to the tissue beneath, but yet can with impunity be swallowed when diluted with water.

We may likewise pass to other material that exercise special influences, but where, so far as we know, artificial habit-forming methods have no part. *Rhus toxicodendron* both excretes a substance and carries a volatile something that produces violent toxic action on some persons, while to others it is as harmless as bedewed grass. A waft of air over the dew-covered vine may close the eyes of a strong man exposed to its air-wafted influence, may cover his body with a most painful eruption, may drive him to seek his physician's aid.<sup>2</sup> Another man or a fragile girl comes next and with impunity, with bare hands, pulls the vine from its fastenings. The eyes of the first man may be closed by the attenuated "poison," imperceptibly attenuated by the gentle breeze, beyond the chemist's art to indentify, while the other person, bespread with its juice, has not even a pimple on his hand. Thus, "poison ivy" is, or is not, a poison, as the individual is or is not susceptible to its influence.

As an illustration, the writer each year has laboratory use for many thousand pounds of *rhus toxicodendron* (poison ivy). The green leaves, when in their prime, are gathered by collectors, who in midsummer, with bare hands and arms, strip the vines, crush the green leaves into sacks, and deliver the product with impunity. No immediate, or after-effect, is noticeable. One young lady of the laboratory force is so sensitive to the action of the drug as to respond to the emanations, although she be in a distant part of the establishment. To bottle and label "*Rhus*," or otherwise handle a preparation, means to her typical *rhus* poisoning. Consequently, at such time, she has a vacation, not being allowed within the establishment.

Once we knew a man to be vaccinated with a virus-crust that, used in equal amount on others, produced no untoward action. And yet that man came near losing his arm. It is evident that not the virus, but the man, or some undetermined local cause connected

with his case, was then at fault. The *virus* was the actual disturber. Let us not overlook that in such cases as these local conditions, such as the syringe needle or skin uncleanness, may be at fault, not the virus.

Physicians may recall the use of a hypodermic syringe from season to season, with no complaint. Then, in the course of ordinary injections, a patient is "poisoned" by the same dose of the same medicine previously employed, and injected with the same syringe needle. The question arises, what caused this exceptional action? Blame is likely to be attached to the virus, regardless of its innocence.

One might fairly imply that either in this one case the syringe needle was infected, or that a shred of foreign matter was injected, or that this one patient was exceptionally sensitive to the remedy employed. Vaccines are not in our sphere; we make no claim to capacity to speak as an expert in this field. But yet letters from patrons citing exceptional experiences in these directions lead us to accept that where one person, and only one, experiences such exceptional results with a preparation where hundreds of others find no untoward effect, the cause may be accepted as local or systemic, its exceptional action lying outside the preparation used. Such as this is a problem for serious study.

Full well is it known that tobacco is destructive to the life of most insects, and yet there are worms that thrive on the green leaf, as well as insects that thread the dried drug, and delight in the choicest cigars. To the one, green tobacco, to the other, dried tobacco, is a food. And yet, this writer was made "deathly sick," as frightened observers can testify, when a film of collodion containing a fraction of a drop of nicotine was painted back of the nail, on the first joint of his thumb. Within a few moments alarming results followed, the poisonous film was at once washed off with chloroform, ammonia to the nostrils and stimulants internally being promptly administered. And yet, without any untoward influence, thousands of employees breathe with impunity the close air of tobacco warehouses, cigar factories, and constantly handle strong nicotine tobacco leaf.

Capsicum, in substance, is heroic, as all who have experienced its direct action will testify. But yet a beetle (undetermined, so far as we know), feeds on powdered capsicum, and burrows in its depths. To that insect capsicum is a choice food, and to the Mexican, in excessive amounts, it is but a pleasant condiment.

The plant known as *sanguinaria* (blood root) contains large

amounts of energetic alkaloids that vomit man, when taken even in small doses. And yet a single mole exterminated a bed in which this essayist took much pride. At least, by circumstantial evidence, the mole got the blame for the offense.

In like manner, biologists are aware that heroic poisons fail to act with some animals, while substances "not a poison" are destructive to others.

"Chambers" is authority for the assertion that natives of Africa drive hogs through serpent-infested sections, the hog not being susceptible to the virulence of that viper. It is stated that the beast presents its cheek to the serpent, then grasps the reptile in its mouth. Tradition has it that the hog is likewise immune to arsenic. Country people have a tradition that a full pail of milk from a newly-calved cow will kill a hog. The father of this essayist doubted the statement and fed a valuable hog a full portion of the first milking. The hog died that night. Seemingly, the experiment succeeded. And yet the cheese made of the first milking of the "nannie goat" commands exceptional value in Smyrna.

The miasmatic fog that catches one person may fail to affect neighbors equally exposed. A plague may sweep away a multitude and yet miss an individual member of that multitude.

Thus we find that the term *poison*, whatever the dictionary definition may be, carries undercurrents of opportunities for questionings, as well as investigations, that make the answer to the question, "*When is a poison not a poison?*" more of a problem than a cursory glance would indicate.

And yet, since, as a rule, such peculiarities as these are exceptional, a cause for each exception unquestionably always exists. The *reason* therefor, in obscured conditions, is an opportunity for science research, the facts having, as a rule, been incontrovertibly established by empirical record. The man of experimentation, opportunity and thought has surely, here as elsewhere, accomplished his share in the chain of progress when he hands to his co-laborer a statement of fact based on balanced observation.

\*From *Eclectic Medical Journal*, April, 1920.

<sup>1</sup> Definition—Poison: "Any substance applied to the body, ingested, or developed within the body, which causes or may cause disease."—DORLAND.

<sup>2</sup> The remedies offered as "poison ivy cures" are legion. This writer believes that the action is often remote from the drug attack. The chain of systemic reactions that produce the body-bred toxins may be likened to the Biblical "third and fourth generations."

## THE PRESENT STATUS OF COMPULSORY HEALTH INSURANCE.

REPORT OF THE COMMITTEE ON SOCIAL INSURANCE READ AT THE NINTH ANNUAL MEETING OF THE AMERICAN DRUG MANUFACTURERS' ASSOCIATION HELD AT THE HOTEL BILTMORE, NEW YORK CITY, APRIL 12-15, 1920.

This being an off year, legislatively speaking, there isn't much to report regarding the movement for compulsory health insurance. During the past winter, interest has very largely centered right here in the State of New York. As a matter of fact, indeed, the leaders of the movement have largely concentrated their forces on New York ever since they were so effectively defeated in California two years ago.

### COMPULSORY HEALTH OPPONENTS GAINING STRENGTH.

There is now pending in the legislature of this State a bill providing for the realization of compulsory health insurance. This is the fifth annual measure of the kind. Last year the struggle was most dramatic. It looked for a week or two as though the proponents of compulsory health insurance would triumph, but the day was finally saved. This year it would appear that the opposition is much stronger. We gather from what we are able to learn that the present bill is not likely to succeed. Not only are its opponents much better organized and far more powerful, but the legislature seems to have troubles of its own and the Davenport measure has become more or less of a side issue.

New York State, indeed, is admirably organized against this fanatical movement. The Merchants' and Manufacturers' Association, with which our body has been affiliated, has carried on a very effective campaign of education. The New York League for Americanism has likewise stepped into the breach and has done most effective work in showing up the sophistries and fallacies of the scheme. And the three groups most directly affected, namely, the physicians, dentists and druggists, have here and there throughout the State coöperated in the establishment of "guilds" and have fought compulsory health insurance tooth and nail.

These "guilds" did heroic work last fall. During the campaign just prior to the November election, a working committee was appointed in each assembly district composed of two physicians, two druggists and one dentist. Each committee called on the candidates

for both the Assembly and the Senate to ascertain their views with reference to compulsory health insurance and to ask for a pledge of opposition to any bill providing for such insurance. A fight was promptly waged against those candidates whose views were held to be contrary to the public interest, and the result was that ten of them went down to defeat. This furnishes one reason why the legislature this year is not quite so keen for compulsory health insurance as it was last.

Passing by the situation in New York State, it may be said, as we have already intimated, that the issue has not elsewhere been a very active one during the past winter. New Jersey seems at the moment to be in favor of compulsory health insurance, but the "guild" idea is being developed in resistance to it, and the history of New York State will doubtless be repeated. Pennsylvania has agitated the subject, but has done nothing acute. The sentiment for such insurance in Ohio, under a little stimulation from Governor Cox, is rather favorable to the scheme. Indiana has a commission at work, but it is apparently not active. Wisconsin has entertained some discussion of the subject, but has apparently not gone beyond the debating stage. The issue has been a fairly live one in Minnesota, where it forms a part of the propaganda involved in the so-called Non-Partisan movement, but nothing is threatened for the immediate present.

So much for the situation at the moment. Now a few words about the character of the movement in general. These questions are frequently asked: Who are the advocates of compulsory health insurance? What sort of friends has the scheme got anyway? How active are they? What is the danger of success?

#### WHO ADVOCATE COMPULSORY HEALTH INSURANCE?

We should say, after a pretty careful study of the movement compassing several years, that the advocates of compulsory health insurance divide themselves very naturally into the following classes:

1. The original group of academic doctrinaires and sociologists. These men for the most part are university teachers, and they sincerely believe themselves to be right. Unfortunately, as Samuel Gompers says of them, they are not open to conviction. They are zealous fanatics.

2. The governors and legislatures of certain States tinctured with socialism, especially the western group of States now carried away by the misbranded Non-Partisan movement.

3. The modern bolshevists who are out for anything that promises to foment class hatred, promote chaos, curb production, destroy prosperity and kill private initiative.

4. The men in every State who have the nose of a hunting dog for political jobs, and who see the vision of a great organization feeding at the public treasury.

Thus we find compulsory health insurance with a peculiar assortment of friends. It is at once to be observed that, not the lion and the lamb, but the zealot and the crook lie down together. Not politics only, but socialistic "reforms" as well, make strange bed-mates.

In the early days of the movement it was thought that the medical profession was in favor of it. For a time the medical profession, indeed, was in favor of it. But now we find physicians arrayed strongly among the opposition, and we observe them to be well organized in one or two States where the issue has reached the stage of practical danger. In this State, for instance, you will see medical organizations resisting the movement to the last ditch.

#### LABOR OPPOSED TO COMPULSORY HEALTH INSURANCE.

The various groups in favor of compulsory health insurance all unite in declaring that it is primarily for the benefit of labor. But the somewhat amusing and certainly very effective answer is that labor itself doesn't want it. It is true that a few scattered units of labor, here and there, have at times been in favor of compulsory health insurance, but the great body of the rank and file, as well as the national officers of authority, are vigorously in opposition. As recently as January 30, of this year, at a meeting here in New York of the National Civic Federation, Samuel Gompers made the following statement:

It has come to me that recently some person has declared that Gompers has been won over to compulsory health insurance. I have already made my answer, which is that I am unalterably opposed to it.

We may be perfectly sure that Mr. Gompers and his associates would definitely align themselves for compulsory health insurance if it were something beneficial to the laboring man. These men are in favor of several movements in behalf of the laborer which capital is resisting. Surely here is something that labor would want if labor found it desirable. The opposition of Mr. Gompers and other leaders is perhaps the most staggering thing which the proponents

of the idea have to face. It also sounds the death-knell of the hopes of those philanthropic doctrinaires who really think they are doing something for the benefit of the human race. They can't effectively push a "benefit" down the throats of union when labor itself has its mouth closed and its lips locked.

Nevertheless people who are in favor of a particular panacea always find it difficult to listen to reason. Mr. Gompers in the speech to which we have already referred went on to declare that "no matter how convincing would be the proof that compulsory health insurance is impracticable and impossible, there would still be those who would not change their position in the slightest degree, but who would still want it." In other words, they are not open to conviction. The doctrinaire doesn't want to be convinced and closes his mind against it. The self-seeker doesn't care whether he is convinced or not: he is of the same opinion still for reasons of profit.

#### COMPULSORY HEALTH INSURANCE FAILS IN ITS PURPOSE

As a matter of fact, indeed, the only excuse for compulsory health insurance is that it would reduce the total amount of sickness on the one hand, and on the other would give the workman medical attention at a reduced cost. Experience in Europe has abundantly proved that compulsory health insurance does neither. As a committee of the Medical Society of the State of New York pointed out last November:

There is no uncertainty about the evidence that the relative morbidity rate infant mortality rate and maternal mortality rate, has been much more materially reduced in the United States during the past twenty years than it has been in Germany and Austria, where compulsory health insurance not alone, but the whole scheme, including invalidity and unemployment insurance and old age pensions, have been in force. It can, therefore, be seen that compulsory health insurance as such plays a very small part in the reduction of length and severity of illness, and that on the whole it has been of extremely little value, medically, in those countries; while it has been the cause of a profound deterioration in medical service and medical morale. Even in England, where it has been in operation for a comparatively short time, it has proved so defective and ineffective for the purposes for which it was instituted that it is now proposed to inaugurate the plan of State medicine to supplant it.

Compulsory health insurance fails not merely to bring the benefits for which it is urged. It actually results in detriment to the public welfare. It is plainly prejudicial to the public interest, and

we sincerely trust that the more it is studied the more this fact will sink into the consciousness of the nation.

#### VOLUNTARY EMPLOYEE INSURANCE THE REMEDY.

At bottom, of course, there is some modicum of sense to be found in the movement for compulsory health insurance. Agitations of this sort are not all bosh and moonshine. The difficulty always is to separate the real from the unreal—the wheat from the chaff—the desirable from the undesirable.

Compulsory health insurance, as advocated by its friends, is simply impossible. It would do far more harm than good. But it may be possible to strip the movement of its evils and get down to the kernel of truth residing somewhere in the heart of the situation. It is perhaps undeniable that some means of insurance protection against sickness should be afforded to certain groups of people. How can this be afforded wisely and rationally?

Mr. Dunning has made a survey of the conditions existing in the plants of our members, and his findings are printed in connection with this report. It will be seen that already manufacturers are groping their way in an effort to deal with the employee in a way best calculated to protect both him and the employer. It may be explained also that during the last few years insurance companies have offered manufacturers a type of protection considerably in advance of group insurance in its original form. Originally group insurance covered death losses only, but it is now possible to buy protection which covers sickness as well.

The insurance companies are earnestly engaged in studying the whole problem, but they find it a complicated one. The laws in the different States are very confusing, and it is exceedingly difficult to suit any one form of insurance to differing conditions and requirements. The general aim seems to be to get up some form of group insurance which will cover everything not taken care of under the State compensation laws. Evidently, as appears from Mr. Dunning's survey, some of our own members are already buying insurance of this sort. Ultimately, no doubt, the manufacturer who desires to protect both himself and his people against losses from sickness will find it possible to get just what he wants at a reasonable cost, and when this time comes the solution of the problem will have been realized.

For voluntary insurance is one thing, and compulsory insurance



is quite another. Voluntary insurance can be economically handled. It will be subject to the laws of competition. It can be purchased by each manufacturer to suit his own particular requirements, and used by him just as long as he finds it beneficial. Compulsory health insurance, on the other hand, drags a long train of evils behind it. It involves an expensive and inefficient organization. It means incompetent and underpaid medical service. It means cheap drugs. More than anything else it means compulsion—and compulsion is repugnant to the free spirit of America. Compulsory health insurance has never yet, in any country where it has been adopted, worked out to the satisfaction of the impartial student, but voluntary insurance may well be contrived which will meet the situation as far as it ought to be met.

Just how far, however, efforts to establish voluntary health insurance will head off the movement for compulsory health insurance remains to be seen. The latter is being pushed with an astonishing amount of vigor. It is apparently gaining strength year by year. Fortunately, however, the opposition is likewise gaining strength, and it may be safely predicted that the battle will be waged more or less fiercely for a number of years to come. We must all of us be on our guard in order to head off a German-made propaganda which would do infinite harm to America if it ever gained a foothold on our soil.

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#### A SURVEY OF EMPLOYEE INSURANCE CONDITIONS AMONG MEMBERS OF THE AMERICAN DRUG MANUFACTURERS' ASSOCIATION.

BY H. A. B. DUNNING.

Thirty-two of the fifty-six members of the American Drug Manufacturers' Association answered our questionnaire in reference to their policy relative to the protection of their employees against loss of income through sickness, ill health or misfortune.

Twenty-seven members stated that they had no form of insurance for their employees against loss of income through sickness, ill health or misfortune. Five companies have some sort of protection, either for the employees or among the employees, only one, however, having anything that approximates a mutual relationship. In this instance, one of the plants of the company has group in-

insurance against sickness, ill health or death, the company paying one-half of the premium for such employees as desire to pay the other half and derive the benefit.

#### EMPLOYEE PROTECTIVE ORGANIZATIONS.

The employees of four companies have protected themselves more or less independently of their employers. In one instance, the employees have a death benefit fund, to which each member, upon joining, pays the sum of one dollar, and subsequently is assessed one dollar upon the occasion of every death within the organization. This is strictly an employees' organization.

The employees of another company have developed a very complete system of insurance, which they call the Mutual Aid Society, and which exists for the benefit of factory workers employed at hourly rates. Any such employee is eligible to membership, and dues are paid according to the amount of benefit desired, the monthly dues being five per cent. of the sum received per week in case of sickness. The amount of compensation is governed by the amount of wages earned per week. Any member of the society may insure in the grade designated by his salary, or in any lower grade, but not in any higher. No member who has not belonged to the society for one month may receive any benefit in the case of absence. Should the company continue to pay wages to an employee during his absence, no benefit is paid by the society. Benefits are paid for a period of not more than eight weeks in any consecutive twelve months. In the case of deaths, the sum of fifty dollars is paid by the treasury of the society to the person or family designated as the beneficiary.

In another company, the employees have an organization in which, for a nominal fee paid upon joining, members are protected in the event of illness, for a period not exceeding twenty-six weeks.

In another instance, there exists a Relief Fund, the disbursements of which are controlled by a committee of employees elected by fellow employees. There are no regular dues, but the weekly bonuses paid by the company to those who have not been tardy or absent during the week are turned over by the company to the fund. In cases of illness, the employee may draw upon the Relief Fund for money, which is generally considered as a loan, and is paid back upon his recovery, although in some cases, where this is impossible or would involve undue hardship, the sum is given outright.

#### PAYMENT OF SALARIES DURING ABSENCE.

Of those companies which have no plan of insurance for employees, six pay full salaries unconditionally during absence due to illness. The general tendency of the majority, however, is to be governed by the conditions of each individual case, and the feeling seems to be that any hard and fast rule is liable to inflict a certain amount of injustice. Full salaries are paid by five companies to salaried employees, office workers, heads of departments, etc., but in all except one of these cases, laboratory employees or others working on an hourly basis of payment, receive no pay whatever during absence. Two companies, while not paying full salaries during absence, pay all doctors' bills for the employee who is sick. In another company, each office employee is allowed thirty days' sick leave throughout the year, and receives extra pay for whatever time is not used out of this allowance, there being no pay during the actual time of absence. One company in a State which requires State compensation insurance, pays the difference, in cases of sickness, between the amount allowed by the State, which is two-thirds of the weekly salary, and full pay. Only one company makes no provision at all for absent employees.

Of those companies which do not pay full salary during absence, one pays eighty per cent. of the weekly salary, one pays one-half, one makes absolutely no allowance, three pay half or full salary, dependent upon conditions, and eight are governed by circumstances as to what portion of the weekly salary is paid during such absence.

In regard to the length of time during which some sort of pay is given by the companies to absent employees, there was a wide variation. Here again, the individual case governed the course followed by many, and length of employment, value of the employee to the company, and the amount of salary received are determining factors. Fourteen companies replied that they were influenced by these considerations. Two companies continue to pay salaries indefinitely, so long as conditions justify their doing so. Two companies pay no longer than a period of two weeks; two pay no longer than three to four weeks, unless unusual conditions warrant it; the Mutual Aid Society above referred to allows compensation for a period of not more than eight weeks during each consecutive twelve

months; the employees of another company are protected by themselves for twenty-six weeks. One company continues to pay salaries for three months, but no longer, while two others pay for a reasonable time. Two companies continue to pay salaries until the recovery of the employee, and only one makes no provision at all.

There was a marked difference of opinion as to how long an employee must have been with a company before he is entitled to pay during absence. Five companies make no requirement of such previous service whatever. Eleven replies state that there is no general rule, although length of service is a determining factor in their course of procedure. There is a requirement of thirty days' membership in the Mutual Aid Society, and the company whose employees have organized this society requires an office worker to have been employed for six months before any allowance is made for absence. Two firms require employees to be with them for three months before paying salaries; three firms have a requirement of one year's service. 'Two years' service is required by another company while five years or more are required by still another, although exceptions to this unusually strict rule are made.

In conclusion, five companies suggested that they would be glad to receive any assistance possible from the Secretary to enable them to work out the problem of employees' insurance, to which they have been giving considerable thought. One company stated that in its opinion any general policy to govern such instances would be unfair, as the circumstances of nearly every employee's absence are different, and that some injustice would probably follow an attempt to make all cases conform to the same rule. Another company suggested some form of insurance to which both the employees and the company would contribute, thus dividing the responsibility and increasing the feeling of mutuality between employer and employee. Group insurance covering death but not sickness was the suggestion of another company, as the payment of salaries during the period of absence takes care of the employee without developing the paternalistic attitude.

HARRY B. MASON, *Chairman.*

F. M. BELL,

H. A. B. DUNNING,

E. H. NELSON,

J. H. FOY.

## GREAT POSSIBILITIES IN THE ASSOCIATION'S LATENT POWER.

REPORT OF THE SECRETARY, W. J. WOODRUFF, AT THE NINTH ANNUAL MEETING OF THE AMERICAN DRUG MANUFACTURERS' ASSOCIATION AT THE HOTEL BILTMORE, NEW YORK, APRIL 12-15, 1920.

This year's report of the Secretary is inspired by a conviction that has been growing firmer in his mind for some time. If I may be permitted to indulge myself in a home-made text for my sermon, let me offer this—"The horse in the barn doesn't turn any furrows." To be less figurative, your presumptuous Secretary believes that, while the membership, with industry generally, is complainingly permitting itself to be seriously hampered by adverse influences, it possesses vast potentialities for correcting those evils of which it is not availing itself.

### GREAT LATENT POWER.

It is safe to assert that, with the single exception of the Proprietary Association, no single factor in the Drug Trade or Medicine possesses the potential power for remedying its evils that this industry possesses. It is likewise safe to say that no industry is using so small a proportion of its potential power in its attempts to meet its problems.

The fact that an association represents a manufacturing industry implies powerful reserves of organization experience—of big caliber men—the association can say the last without immodesty for men who manage such great units can be nothing else—and—but here I must focus my meaning well—if I mention capital as a source of power, I do not mean to imply its use as a force for coercion, corruption, undue influence or suppression of truth or justice, or for any other use immoral or even unethical. I mention it rather for the legitimate uses to which it can be put, uses in no way inconsistent with the public welfare. We could be charged with nothing worse than a desire to have justice done us if we used it, let us say for the dissemination of truthful information that would make the public proof against the misrepresentations of either those with ulterior motives or of well intentioned but ignorant reformers.

The A. M. A. has long been regarded by many in pharmaceutical and medical circles as the dominant factor in these fields, with

almost irresistible power for bringing the other factors into absolute subjugation, if it should ever will to so exercise its strength, which I am not contending. Yet, why should this be so? Their organization, it is true, has the advantage of many years more building than has our own, but it is nothing that could not be easily duplicated were the organization experience of the membership applied intensively to the task. And outside of this, the natural advantages are with this association. It cannot be said that the financial resources of the A. M. A. are anywhere near as great as those of this industry. And it must be admitted that their organization lacks the coherency of one with our smaller and more compact membership. The interest of the average physician in the A. M. A. is only general in character. The A. M. A. can only deal with problems that affect him indirectly in a scarcely palpable way and besides he is not likely to be in sympathy with all its decisions. It would be a physical impossibility for an organization with better than 50,000 members to reflect the sentiment of the individual as accurately as does our own association of from fifty to sixty members, and to reflect it, moreover, 99 times out of a hundred. The so-called advantages of its members are in my judgment negatived by the disadvantages. What elements of strength its numbers do possess are offset, it seems to me, by the fact that you cannot compare the influence of a single individual physician with that of a manufacturing establishment such as goes to make up our membership.

There is nothing that the A. M. A., or any other Association, has done or can do that we cannot equal, or—if their activity is adverse to our legitimate interest—offset, if the industry is only of a mind to devote a fair proportion of its resources of brains and money and experience to the enterprise. Let me put you at your ease. This is not a preface to the submission of some proposal involving vast expenditures. I am not coming to you with a proposition on which I expect you to act at this meeting. It is simply my intention to put to you more concretely than I have done before some of the constitutional remedies that appeal to me as cures.

If, acting on your own initiative, you should ever see fit to adopt them, they would call, it is true, for much larger sums than you have been in the habit of expending on Association activities. Their proportion to the sales of the industry, however, would be trifling compared to the proportion that an advertising appropriation of reasonable size bears to the advertiser's annual gross sales, and the

good they would accomplish would make the expenditure an even more profitable investment.

#### THE ADVERTISING OF EDUCATION.

In past reports I have hinted in perhaps rather vague terms that this industry needs a good constitutional tonic in the shape of a more accurate public conception of its importance and a more sympathetic understanding by the public of its problems. In the belief that the membership have grown sufficiently strong in the coöperative spirit to perhaps lend me a sympathetic ear, I intend now to speak more concretely and pointedly on this subject. I hope whatever reputation for level headed judgment I may possess will not suffer. To speak frankly rather than modestly I don't think it should. If my ideas seem radical, then I am in the same boat with the best brains of many other representative industries of the country for they are doing what I believe this industry should do. They are coming out openly as becomes honest men, and are using the advertising columns of the newspapers and periodicals to portray for the public their ideals and their problems and the interest that the public has in their welfare.

This is not the advertising of buying and selling; it is the advertising of education. Those who are advertisingly near sighted and conceive of advertising simply as a medium for telling the reader you have something to sell should put on glasses that will enable them to see the bigger field beyond in which advertising loses its commercial character and takes on the guise of an educational force that commands respect and silences critics.

We find a host of industries using it as means of broadening the vision of the people as to the useful possibilities of some utility, and thus increasing the market for that utility as a whole without reference to a particular brand. In this undertaking are enlisted the orange growers, the manufacturers of white pine, and a number of other industries whose names I do not recall. This advertising has a commercial aspect, it is true, but it has not a selfish aspect for, to increase the public knowledge of the uses of white pine, for instance, benefits all manufacturers and growers of this lumber regardless of membership in the Association under whose auspices the advertising is conducted.

But the faintest taint of commercialism cannot be attributed to that phase of advertising that is dedicated solely to the purpose of

cultivating a better public appreciation and understanding of an industry and the country's interest in its welfare. We find the packers, the telephone companies, the Ayer's Advertising agency, and, a recent recruit, the National Canners' Association, to say nothing of many others, all maintaining advertising campaigns of this character. Were you to read one of the better types of advertising copy of this class in other than the make-up of an advertisement, you would be more inclined to suspect it of being a portion of an article from the reading columns, written by some disinterested party, so restrained are they apt to be in their references to the industry in whose interest they are published and so commendable are many of them from the standpoint of literary criticism. You might be impressed by the new and greater conception of that industry that the imagination of the copywriter imparted to you by figures of speech that would do credit to an author of literary pretensions, or you might admire the rich fancy of the artist who illustrated the text with a finesse akin to that of a master of the academy. You would find in short an appeal to your cultural rather than to your commercial sense.

To make my meaning more clear by example, just consider the following copy that appeared in an educational advertisement of the Telephone Company but which might just as well have formed a part of an essay.

"Cave Life or Civilization.

"Civilized man is distinguished from the cave man by his habit of coöperation.

"The cave man lived for and by himself; independent of others, but always in danger from natural laws.

"To the extent that we assist one another, dividing up the tasks, we increase our capacity for production, and attain the advantages of civilization.

"We may sometimes disregard our dependence on others. But suppose the farmer, for example, undertook to live strictly by his own efforts. He might eke out an existence, but it would not be a civilized existence nor would it satisfy him. He needs better food and clothes and shelter and implements than he could provide unassisted. He requires a market for his surplus products, and the means of transportation and exchange.

"He should not forget who makes his clothes, his shoes, his tools, his vehicles and his tableware, or who mines his metals, or who



provides his pepper and salt, his books and papers; or who furnishes the ready means of transportation and exchange whereby his myriad wants are supplied.

"Neither should he forget that the more he assists others the more they can assist him.

"Take the telephone specialists of the Bell System: the more efficient they are, the more effectively the farmer and every other human factor of civilization can provide for their own needs and comforts.

"Or take our government, entrusted with the task of regulating, controlling and protecting a hundred million people. It is to the advantage of everyone that the government shall be so efficient in its special task that all of us may perform our duties under the most favorable conditions. Interdependence means civilized existence."

#### EVADING THE PHYSICIAN'S PREJUDICE.

It has long been a belief of the ethical medicinal manufacturer that, since his sales leverage is on the physician, any advertising of a popular nature would be a lethal dose to his business. Like a good many other business traditions, it has been accepted as an axiom unnecessary of proof. A little effort to think all around the subject would, I believe, dethrone it from this position just as many other so-called business axioms have been dethroned by some hewer of new trails who has made an undreamt of success largely because he disregarded the rules of the game and played it in a new way.

The ban of the medical profession against advertising to the public is based on the very laudable principle that the calling of the physician is too noble to be made a subject of commercial exploitation. It was imposed in the days when advertising was a crude thing of "best on earth" boasts in brazen and ugly display and when a business man had no other vision of advertising than as a medium of telling greater numbers than his salesmen could reach that he had something that he wanted them to buy. It is the very antipodes of the educational advertising of the sort proposed here, advertising that seeks only to enlighten and whose physical nature is commendable from both literary and artistic standpoints. The prejudice of the physician against advertising that goes to the people should not be regarded as a rock that absolutely bars the passageway. It may be a rock but there are plenty of passages around it, and it is

only a case of steering wisely to evade it. It simply means that care must be exercised to avoid the slightest exaggeration, the slightest misstatement, the slightest suggestion of idle, boasting, or the slightest tendency to lower the dignity of the medical profession or to commercialize human suffering. These are negative virtues and, not content with their observance we should seek to impart qualities to our advertising that would positively tend to win the commendation of the physician.

Copy of a restrained tone written in a style that would reflect lofty sentiment could not do otherwise than impress him favorably; neither could an illustration artistically picturing some of the nobler aspects of the physician's art, or some altruistic phase of medicinal manufacture. And if the advertising treated of the whole cycle of the healing art, the physician, and the pharmacist, as well as the manufacturer, picturing to the people the public service the physician and pharmacist renders, your advertising would not only be unobjectionable to him but it would be a positive agency in cementing his goodwill, and the goodwill of the druggist as well.

#### STYLE OF COPY RECOMMENDED.

And now let me give you a concrete illustration of how such copy as I have described could be used to cultivate a sympathetic public attitude and at the same time the goodwill of the physician and the druggist. It is hurriedly written without due consideration of the points of which the first advertisement should treat, and falls far short of literary merit but it serves to illustrate the style that I am trying to explain.

When the faint glow of the last ember of life brightens under the ministrations of the physician at the bedside, and your loved one comes back to you from the brink of the Great Shadow, your heart, for the first time, wells up with all the gratitude that this, humanity's greatest earthly friend, deserves.

You repay him then in speechless thankfulness for his sleepless nights of watching, his midnight hours of study, and the sunny holidays of youth spent in sombre college laboratories. And in your gratitude, think sometimes of his silent partners—the workers to whose tireless research and exacting care are due the contents of the bottle with which the magic was wrought.

The genial proprietor of the corner drug store may seem simply an obliging merchant to whom you are indebted for a hundred little

services, but he, too, is a professional man—a pharmacist who has paid his toll in arduous study. Had he erred in the pharmacist's delicate, hairline task of filling the prescription, the physician's skill might have only served to mend the ravages of your passionate grief.

And behind the physician and the druggist is the great army in the manufacturing establishments in which the ingredients of the prescription were made. The bacteriologists, the pathologists and the research chemists who, in the face of a weary chain of failures, developed and perfected the formulas. The financial captains who unflinchingly watched thousands upon thousands of dollars sunk in fruitless experiments before the first glimmer of success. And the workers who throughout every step of the transformation of the crude chemicals into the finished preparation tested and retested its power and purity.

#### SUGGESTED FACTS.

You observe that I would rely on indirect suggestion to get my points home rather than on the force of direct statement or argument. It is because facts that are implanted in the reader's mind subconsciously by force of suggestion are less likely to be challenged by him than are those which are stated baldly to be facts. As for argumentative copy, its use immediately puts the reader in an argumentative frame of mind and he is very likely, from the sheer contrariness of human nature to take the other side.

In the last paragraph it is the intention to awaken the reader to two facts which I believe are contrary to the prevailing impression—first to the fact that the plant of the medicinal manufacturer is really a scientific laboratory and his force composed of scientific experts, and second to the fact that it is to the medicinal manufacturer that Medicine owes a big share of the progress in the development of remedial agents.

In the manner in which these points are here stated their acceptance by the reader is assumed and this very fact tends to induce him to accept them under the impression that nobody questions them. Were the entire five paragraphs to be devoted to proofs of the truth of these propositions, it is doubtful if the reader could be induced to accept their verity as readily. The very fact that you deemed it necessary to prove them would cause him to reserve judgment under the impression there are "two sides to the story."

The latter method, it is true, would leave no question in the mind

of the reader as to what you are "driving at," and, conversely, it is true that the methods used in the copy, being less obvious, might cause the meaning to escape more persons than in the case of the former. But the secret of successful advertising is the repetition of the same thought in a number of fresh ways until continuity of impression has firmly implanted it in the mind of the reader, and if you can get your idea home without stirring up doubt your task in the end will be a shorter one.

#### AIMS OF THE CAMPAIGN.

Every advertising campaign that hopes for conspicuous success should be carefully planned from beginning to end before the first piece of copy is written. Its aims should be carefully defined and every individual advertisement should be prepared with that aim in view, in order that each may contribute to the continuity of impression that means advertising success. What the points should be in the first campaign of this industry is a matter for careful discussion. I would venture the suggestion however, that

1. It should explain the mission of each of the principal factors in the drug and medical worlds and endeavor to impress the public with their worthiness and their vital consequence. This would make such a campaign seem more altruistic and help to instill in the public an impression that the industry is inspired by other than purely selfish motives. It would, moreover, increase the goodwill of these other factors for the industry and would serve to contribute to.

2. The second aim which is to awaken the public to the fact that the remedial agents of the medical profession do not "just grow" but are the product of a distinct industry.

3. Thirdly, it should impress the people with the fact that this industry is imbued with the ideals of the medical profession and that while it is naturally looking for a reasonable profit its zeal to serve the public and the profession will brook no sacrifice in quality or service.

4. That it is to the medicinal manufacturer that Medicine owes the development of its medicinal agents, and

5. That there is no industry in whose welfare the average individual has a greater interest, that undue restraint on its liberty of action hampers one of the biggest factors in medical progress, and that it

is to the interest of the public to safeguard its production in times of embargoes, shortages and other adverse conditions.

#### SIZE OF THE CAMPAIGN.

It would of course be neither feasible nor wise to attempt a campaign of the dimensions of the Wrigley's three million-dollar per annum appropriation. Nor would it be positively necessary to resort to a campaign of the size employed by the Telephone Company or the Cannery Association. The industry could feel its way, always remembering however that there is a minimum beneath which its advertising effort would not be worth the ineffectual results accomplished. Of what that minimum consists is a matter for careful consideration. I would suggest the following however as the most conservative campaign from which justifiable results could be expected. There should be selected the six representative national magazines of general circulation which would cover the country as adequately as possible. The industry could contract for six insertions in these magazines for the year to be alternated so as to give it three insertions in three magazines one month and three in the second trio the following month. Your advertisements would thus follow each other at monthly intervals and this would mean that a large proportion of your readers, those, in other words, who read two or more of the magazines in question would be reached every month.

The amount of space taken should in your Secretary's judgment be a full page. This space tends to give your reader the impression of a large campaign and humanity has great respect for size, attributing to the full page advertiser a place as one of the larger and more representative industries of the country and consequently one whose standing is in some measure a guarantee of integrity.

The full page advertisement likewise has greater proportionate attention value for the page carries no other advertisement with which yours must compete for the reader's attention. It must also be borne in mind that the effect of the admirable lay-out of one advertisement may be absolutely destroyed by that of an adjacent advertisement which does not harmonize with it. Then, too, the full page displays your illustration or your copy to an advantage that is lost in smaller size space. The necessity for the use of larger space increases moreover with a reduction in the number of insertions.

It is not pretended that a campaign of this number of insertions

in this number of mediums would be as effective as a campaign of, for instance, twelve insertions in a larger number of journals, all conditions being equal. But it could be made as effective as many campaigns of twelve insertions in a much larger list of mediums, if careful workmanship and a policy of giving quality the right-of-way were fruitful in producing advertisements of unusual interest and attention value, and also if the six mediums were selected with requisite care.

#### FOLLOW-UP OF THE CAMPAIGN.

The auxiliaries that could be brought to the support of such a campaign are multifarious but there is one that I would particularly recommend. Your magazine advertisements should be calculated to arouse an interest in the reader—perhaps in the form of curiosity—for further information of a character that would further the objects of your campaign. If the advertisements were a success in this respect, we would find our readers impressed in varying degrees at any given stage of the campaign. Some would be just sufficiently interested perhaps to watch for the next advertisement, others would be sufficiently interested to send for a booklet giving promise of satisfying their human thirst for accounts of the mystical or the magical or the unexpected. The very fact that he thinks of alcohol only as a thing of evil would arouse the reader's curiosity in a booklet with some such title as "Our Faithful Servant Alcohol," while others who take umbrage at the loss of their daily glass of beer or wine would be interested in it out of a sympathetic attitude for a friend whom they think is being unduly abused. A colorful but accurate story in popular language of the wonders alcohol performs as a solvent would be of as great if not greater interest than "the story of a grain of wheat" or "the story of a piece of coal" or other popular science stories of their ilk.

In thinking of the distribution of such booklets through popular advertising, you must think in terms of hundreds of thousands. Think of what it would mean to educate such an army to the fact that there is a praiseworthy use of alcohol that must be safeguarded, and if you made proper use of your material you would incidentally develop some one of the fundamental aims of your campaign. To take one of those I have suggested you could in the development of your story of alcohol treat of some conspicuous example of a therapeutic agent developed in the laboratory of the manufacturer and

impress this same army with the fact that the medicinal manufacturer is one of the most important factors in the scientific progress of curative agents.

#### EFFECT OF CAMPAIGN.

In the past years of the Association's existence, I verily believe that the industry has not become known to as many as ten thousand persons outside the medical and pharmaceutical worlds. In one year, a campaign of this character would bring it to the attention, and that in a most favorable light, of hundreds of thousands, if not millions, of people, making them less susceptible to unsound propaganda and less likely to add their voices to the demand for legislation in response to it.

Besides this you have the consideration that magazines are read not only by the rank and file, but also by the bureau chief who formulates the regulation you must follow, by that legislative activating agent of great potency, the public-spirited clubwoman, and no less by the legislator, the editor, the preacher, and a hundred other influential elements in the body politic.

One legislator thus influenced might give your cause a champion sufficiently strong to turn the tide of a legislative contest in your favor and one editor impressed with your important public mission and your worthiness might give your cause the weight of a journal of great influence in molding the opinion of thousands of readers.

You stand to gain not only the benefit of a sympathetic public opinion in the aggregate but also the championship of single elements in that heterogeneous mass called the people whose goodwill can be of great direct benefit to you. Your activities would likewise tend to stimulate a public interest in matters medicinal that would react on the public press and stimulate the publication of articles to your interest, articles all the more influential because they would not bear your stamp.

#### PUBLIC ESTEEM THROUGH SCIENTIFIC ATTAINMENT.

I hope I have said enough on this point of publicity to illustrate that the matter of giving ethical medicinal manufacture an influential and representative place among the industries of the country, a place that will make it proof against the domination of any other force, is simply a question of employing the great latent forces within ourselves that are now lying dormant.

Advertising in national magazines is not the only channel through which these forces can be applied. In fact the imagination can conceive of so many others that it is my purpose merely to cite one or two by way of illustration rather than to attempt to cover them all comprehensively. Let one additional one suffice.

When you consider the years of experience and accumulated data, the wealth of scientific brains, the elaborate organizations of laboratory equipment, and the great advantage of organized capital that is behind this industry your imagination must conceive a rather glowing picture of the leading place that the industry could attain in medical science if it would only make full use of its powers. It is quite true that we have the prejudice of the scholastic scientist with which to contend, but I hope to show that the prejudice is no very formidable obstacle after all.

There are innumerable drugs on which the literature is unsatisfactory or meagre. There are scientific men universally recognized as authorities and whose work on these drugs would at once receive recognition from all factors in the scientific world. In the archives of our members are many years accumulations of invaluable data on these drugs. There are besides some fifty odd laboratories whose coöperation would give a research worker ample corroborative tests.

If the membership were disposed to make full use of its resources the Association could select some problems whose solution would constitute a conspicuous contribution to the science of medicine, it could likewise retain a man of this caliber to devote a year or more of his time to it, and it could give him many years start on a private investigator working alone by placing the experience of its members at his disposal and by giving him the coöperation of these fifty odd laboratories.

His report published under the auspices of the Association and given freely to the world would be accepted on the strength of his name by even those ultra academic scientists who deprecate the work of commercial laboratories.

Conceive of the interest with which a work of so elaborate a character would be received by the Pharmaceutical and Medical worlds and ask yourself if many years would pass before these annual or biennial contributions to science by the American Drug Manufacturers' Association would take their place as one of the most eagerly awaited and most authoritative of scientific series. And, judged in the light of this work, the American Drug Manufacturers' Associa-



tion and the industry it represents would most certainly grow in public esteem.

It is from your Scientific Section that this recommendation, fathered by Dr. Eldred of Eli Lilly & Co., comes and though it may be the most ambitious recommendation ever made by the section it is only in keeping with the scale on which the Association should begin to do things if it would make the most of its possibilities.

The growth in the coöperative spirit in the industry which your Secretary has watched with a good deal of satisfaction during the past four years causes him to hope that the message of this report does not wander too far beyond the confines within which you think the Association should be kept. But if it does, he accepts your dictum with all the good grace of a loyal servant and he hopes in turn that you will pardon his frankness as inspired by a sincere desire to advance the interests of the membership.

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### GOOD DRINKS MADE OF MILK.\*

Milk drinks, made right, are unquestionably good. They are healthful, nourishing and delicious, and when made according to the methods prepared by milk specialists of the U. S. Department of Agriculture, no difficulty should be experienced in marketing them. Following are some methods for making buttermilk, yogurt or Bulgarian buttermilk, buttermilk lemonade and kefir or koumiss.

*Buttermilk.*—In making buttermilk from milk the same procedure should be followed as in making a starter for cream ripening. A good, clean-flavored mother starter should be carried along with every possible precaution to prevent contamination. Good commercial cultures can be obtained, but if it is not convenient to use one of these a natural starter should be secured. For this purpose the following procedure may be followed.

Select milk from several sources; put about one pint from each source into clean glass jars or bottles and allow them to stand in a warm place until the milk is curdled. When this occurs, put about 1 pint of milk into each of an equal number of bottles and hold in steam or boiling water for one-half hour. When these bottles of milk are cooled, transfer about 1 teaspoonful of milk from each of the bottles of sour milk obtained in the first operation to one of the bottles of heated and cooled milk. Allow these samples to cur-

\* From *Pure Food Products*, Feb., 1920.

dle and repeat the process until one sample is obtained which curdles in at least 8 or 10 hours with a smooth curd free from whey and gas bubbles, and with a pleasant acid taste.

Gas bubbles, or the separation from the curd of a milky or straw-colored whey, show that the lactic-acid bacteria are still mixed with other kinds. Considerable variation in flavor can be found in different cultures, and care should be exercised to select one that gives a clean, sharp taste.

Propagate this culture in the same way from day to day. The amount of this mother starter which should be carried will depend upon the amount of buttermilk to be made. One quart should be enough for 20 to 30 gallons.

Add the mother starter to the milk to be used for buttermilk, or pasteurize the milk in a continuous pasteurizer at 180 to 185 degrees F. (82 to 85 degrees C.), or preferably hold the milk in water-jacketed vats or cans at 180 degrees F. (82 degrees C.), for thirty minutes to an hour, cool to about 70 degrees F. (21.1 degrees C.) and add the mother starter. The most desirable temperature for this fermentation is 70 to 75 degrees F. (21.1 to 24 degrees C.).

When this milk has curdled, cool it at once to about 50 degrees F. and churn thoroughly to break the curd into fine particles.

Buttermilk may be improved especially as to its texture and tendency to whey off, by the addition of about 10 per cent. of a milk culture of *Bacillus Bulgaricus*.

*Yogurt or Bulgarian Buttermilk.*—Propagate a small culture of the *Bacillus Bulgaricus* from day to day as indicated for the lactic culture for buttermilk. This culture may be obtained from various commercial laboratories. To prevent contamination by yeasts or gas-forming bacteria, it is necessary to carry this culture at a temperature of about 110 degrees F. A small egg incubator may be used for this purpose.

Carry in a similar way a culture of the ordinary sour-milk organism, which may be obtained from many of the commercial laboratories.

Thoroughly pasteurize the milk to be fermented. If a small quantity—5 to 10 gallons, for instance—is to be made, it may be done by holding a can of milk in a tub or vat of water heated by a steam hose. If a larger quantity is made, one of the starter cans used in creameries will be found convenient. These are essentially cylindrical vats with mechanical stirrers and a jacket which can be

filled with steam for heating or water for cooling. The milk should be held at a temperature of at least 180 degrees F. for not less than 30 minutes.

Cool the milk to about 100 degrees F. Draw off one-half and inoculate it with the culture obtained in the second operation. Inoculate the remaining half with *Bulgaricus* culture obtained in the first operation. The amount to be added will depend on the quantity of milk to be fermented, the time at which it is desired to have it curdled, and the temperature maintained during the fermentation. This can best be determined by experience. One pint should be sufficient for any amount between 10 and 20 gallons.

The milk inoculated with the product of the second operation may be held at ordinary room temperature. Precautions must be taken to hold that part inoculated with the *Bulgaricus* culture at a temperature of 90 to 100 degrees F. for several hours. If the milk is in cans it may be set in a tub of warm water. A large volume of milk in a warm room will maintain the proper temperature.

If one is unable to hold the milk at the desired temperature the amount of culture inoculation should be increased.

When the milk has curdled—which should be in 10 or 12 hours—mix the two lots thoroughly by churning or stirring together, bottle, and put on ice to check the acid formation.

*Buttermilk Lemonade.*—A refreshing and nutritious drink may be made by the addition of lemon juice and sugar to buttermilk, following the same procedure as in making ordinary lemonade. It will usually be found necessary to use more sugar and more lemon juice than in making lemonade with water. Buttermilk lemonade should be served very cold.

*Kefir or Koumiss.*—Use buttermilk or freshly curdled sour milk. This should be thoroughly agitated to break the curd into fine particles. Buttermilk containing *Bacillus Bulgaricus* will give a flavor too acid for most tastes.

Add 1 per cent. cane sugar ( $1\frac{1}{2}$  oz. to the gallon). Add a small amount of yeast cake—one-fourth of a cake will be sufficient for 1 gallon of buttermilk. The yeast cake should be ground up in water so that it will be well distributed.

Bottle this preparation, leaving sufficient space to permit a thorough shaking of the contents. Strong round bottles of the type used for carbonated drinks should be used, as considerable pressure is developed by the fermentation. If the bottle is not provided

with a sealing device the corks must be securely tied or wired in place.

Hold for 4 or 5 days at a temperature of 65 to 70 degrees F., shaking every day to keep the curd well broken up. At the end of this time there should be considerable gas but not enough to blow the milk out of the bottle. It should have a pleasant acid taste with a slight bitterness. The fresh milk sometimes has a yeasty taste, but this gradually disappears. If the milk is kept on ice it will remain in good condition for two weeks or more.

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## CURRENT LITERATURE

### MEDICAL AND PHARMACEUTICAL NOTES.

ESTIMATION OF SUGAR IN BLOOD IN DIAGNOSIS AND TREATMENT.—A study of more than 700 cases of diabetes by Cammidge has shown that there is no constant blood sugar level for the appearance of sugar in the urine in quantities recognizable by ordinary tests; also that there is no definite relationship between the percentage of sugar in the blood and either the percentage or total amount of sugar excreted by the kidneys. Patients with a permanently high blood sugar may pass comparatively little sugar in their urine, while, in some instances, a normal, or even a subnormal, blood sugar curve may be associated with frank glycosuria. In either condition, examination of the urine alone does not give a correct picture of the case, and, if it is not checked by blood sugar estimations under controlled conditions, may readily lead to mistakes in diagnosis and treatment. As a rule, young diabetics have a lower threshold point for clinical glycosuria than those of middle age, and the threshold rises with advancing years. It is, therefore, important that the presence of even small amounts of sugar in the urine of persons of middle age should not be dismissed as of little significance, unless a series of blood tests have shown that their tolerance for carbohydrates is not seriously defective. Hyperglycemia may exist without clinical glycosuria, that is with an insufficient percentage of sugar in the urine to give the ordinary tests for sugar. The reverse condition, glycosuria with a normal or subnormal percentage of sugar in the blood, is not as uncommon as is generally supposed. Cammidge's observations suggest that many cases of latent diabetes are essentially hepatic in origin, and that so long as the patient

avoids sugar and foods containing sugar as such, he may take any starchy food in moderation without harm, provided that the protein and fat content of the diet are also controlled. He warns that too hasty a diagnosis of diabetes should not be made from the presence of an excess of sugar in the blood nor even from an abnormal blood sugar curve after a test meal of sugar, for other diseases may be associated with hyperglycemia. In the later stages of nephritis, for example, the percentage of sugar in the blood is usually high, often equalling the amount met with in severe diabetes when uremia is imminent, but the blood picture is one of complete metabolic failure, and the end products of nitrogen metabolism are correspondingly increased. Some excess of sugar in the blood is usually found in patients suffering from cardiovascular diseases with high blood pressure, even when there is little or no indication of renal disturbance. Carcinoma is another condition in which it is said that there is often moderate hyperglycemia. (From *Practitioner*, London 104: No. 2, (Feb. 1920); through *Jour. Amer. Med. Assoc.*, Mar. 27, 1920.)

POISONING BY OIL OF EUCALYPTUS.—Auerbach reports a case of poisoning in a man of 47 who had ingested about 20 Cc. of oil of eucalyptus. Half an hour afterward he was found unconscious in bed. Auerbach found the patient cyanotic; with a weak, slightly accelerated pulse, and covered with a cold sweat. The pupils were contracted and fixed. The area of cardiac dullness was increased, and breathing was shallow. Ingestion of milk caused vomiting, and milk lavage brought forth distinct evidence of eucalyptus oil. The condition of the patient slowly improved, and complete recovery followed on the fourth day. Auerbach gives this account of the case because he finds in the literature few reports of poisoning from oil of eucalyptus. (From *Deutsche medizinische Wochenschrift*, Berlin, Oct. 16, 1919; through *Jour. Amer. Med. Assoc.*, Feb. 14, 1920.)

QUANTITY OF DIASTASE IN NORMAL URINE.—The urine of 114 persons was examined by Saigusa by the one-half hour method of Noguchi and Wohlgemuth. The quantity of diastase thus determined varied from 8 to 64, in the majority of cases ranging from 16 to 32. It had, to a certain extent, a relation to the specific gravity of the urine. The starch paste used by Saigusa in his experiments was prepared from official potato starch by heating it for a certain time to destroy amylopectin contained in it, and then passing it through a filter. The author claims that this starch paste could

well take the part played by the soluble starch of Kahlbaum in this experiment. (*Jour. Amer. Med. Assoc.*, February 21, 1920.)

PREPARATION OF STERILIZED CAMPHORATED OIL FOR INJECTION.—The 1 : 10 solution of camphor in olive oil, which is widely prescribed in French practice for administration by hypodermic injection, may be easily and effectively prepared as follows: Pure olive oil preserved from contact with the air by means of a layer of alcohol (95 per cent.) is heated in a long-neck flask in a boiling water bath until all the alcohol is evaporated. The oil will be perfectly sterilized by this procedure. The flask is then removed from the source of heat, and when the temperature of the oil has fallen to about 40° C. the camphor is added and dissolved. If necessary, the camphor may first be dissolved in a small quantity of ether. The author has prepared more than 5,000 camphor injections by this method, and has never had a case showing any ill effects following the administration. (E. Cabannes, *Bull. Soc. Pharm. de Bordeaux*, 57: 158, 1919; through *The Pharm. Jour. and Pharm.*, Feb. 14, 1920.)

GUAIACOL AS AN ANAESTHETIC.—Dr. Georges Laurens advises the use of guaiacol as an anaesthetic for the more ordinary operations on the ear, nose and throat. As regards the ear, and more especially paracentesis of the drum, he employs a solution of synthetic guaiacol in oil. The latter should be prepared in the manner recommended by Lucas Championnière. Very pure olive oil should first be treated with chloride of zinc in order to get rid of resinous and proteid substances; then washed with alcohol to remove any fatty acids formed, and finally it should be kept at a temperature of 100° C. for some time. The product thus obtained is extremely pure. Dr. Laurens at first made use of a 1 in 10 solution of guaiacol, but he soon abandoned it in favor of a 1 in 20 solution, as he found that the latter produced quite satisfactory anaesthesia. As regards the technique, he follows very closely that recommended by Dr. Lehmoyez. The ear is cleansed first with tepid sterile water, and then with a solution of carbolic acid. Five or six drops of the guaiacol solution are next introduced into the ear and allowed to remain during 15 or 20 minutes. It is then removed by means of a tampon of cotton wool, so that the passage is quite clear and the operator may see what he is doing. For the operations in the nose and throat, the solution is applied by repeated paintings. The quantity of solution used has

never been more than 2 Cc. It is important to note that anaesthesia is obtained much more slowly than with cocaine. With the latter ten minutes sufficed; but with guaiacol one must wait at least fifteen or twenty minutes. (*Med. Press*, Dec. 31, 1919; through *The Pharm. Jour. and Pharm.*, Feb. 14, 1920.)

DETERIORATION OF CRYSTALLINE STROPHANTHIN IN AQUEOUS SOLUTION.—Experiments were undertaken by Levy and Cullen to ascertain the cause of the deterioration of aqueous solutions of strophanthin in relation to the altered hydrogen-ion concentration, and to advise a method for preparing a stable solution for therapeutic purposes. Many of the glass containers commonly used in the laboratory, and most of the glass ampoules employed in marketing sterile solutions for hypodermic or intravenous medication, were found to yield sufficient alkali on autoclaving, to change the reaction of distilled water from  $p_H$  6.0 to  $p_H$  9.0. This increase in alkalinity is sufficient to render biologically inert and partially to decompose aqueous solutions of crystalline strophanthin in the concentration ordinarily employed in the clinic. It is suggested that for clinical use, crystalline strophanthin be dissolved in 0.02 M standard phosphate solution at  $p_H$  7.0, and marketed in hard glass ampoules, thereby insuring stability of reaction with preservation of biologic activity. (From *Jour. Exper. Med.*, Baltimore, Mar. 1, 1920; through *Jour. Amer. Med. Assoc.*, April 10, 1920.)

## EXTENSION OF GERMAN CHEMICAL INDUSTRY.\*

BY TRADE COMMISSIONER C. E. HERRING.

BRUSSELS, BELGIUM.

That the German chemical industry is determined to regain its former ascendancy in world markets if possible is indicated by a further increase in the capitalization of large German establishments. At a recent meeting of the companies mentioned below, which grouped themselves about two years ago, increased capitalization was decided upon, although the capitalization was also increased when the group was organized. The new issues will bring the total capitalization to 1,073,520,000 marks, distributed as follows:

\* From *Commerce Reports*, December 31, 1919.

	Present Stock Marks.	New Stock Common Marks.	New Stock Preferred Marks.	Total Marks.
Badische Anilin..	90,000,000	90,000,000	72,000,000	252,000,000
F. Bayer & Co...	90,000,000	90,000,000	72,000,000	252,000,000
Hoechts.....	90,000,000	90,000,000	72,000,000	252,000,000
Cassela & Co....	45,000,000	45,000,000	36,000,000	126,000,000
Stede Treptow...	33,000,000	33,000,000	26,400,000	92,400,000
Greisheim.....	25,000,000	25,000,000	20,000,000	70,000,000
Weiler ter Meer..	10,400,000	10,400,000	8,320,000	29,120,000
Total.....	383,400,000	383,400,000	306,720,000	1,073,520,000

## PRODUCTION OF VANILLA IN THE SOUTH INDIAN OCEAN.

BY VICE-CONSUL E. A. FEIBELMAN,

TANANARIVE, MADAGASCAR, JANUARY 19, 1920.

The production of vanilla beans in Madagascar and dependencies, including the Comoro Islands, and in the islands of Reunion and Mauritius for the season 1919-20, has been established as follows:

Madagascar and dependencies:	Pounds.
Comoro Islands.....	403,204
East Coast.....	423,503
Nossi-Be.....	110,230
Total.....	936,937
Mauritius.....	2,646
Reunion.....	198,414

Statistics just received by the consulate from the governor of the Seychelles Islands indicate that the vanilla production in that archipelago is estimated at 6,614 pounds of cured vanilla for the year 1919.—From *Commerce Reports*, March 19, 1920.

## NEWS ITEMS AND PERSONAL NOTES.

DECEASE OF FRANK G. RYAN.—The decease of Frank G. Ryan, President of Parke Davis & Co., at his home in Detroit on April 20th, is announced. An appropriate memoir of this eminent and influential character in the drug trade will be published in an early number of the AMERICAN JOURNAL OF PHARMACY.



FAIRCHILD BROTHERS AND FOSTER SECURE ADDITIONAL BUILDINGS.—The growing business of this well known firm engaged in the manufacture of pharmaceutical specialties, has necessitated additional facilities. They have recently acquired the properties Nos. 70, 72, 74, 76 Laight Street, 413 Washington Street and No. 428 Greenwich Street, New York.

This entire space is to be occupied by Fairchild Brothers and Foster for offices, warerooms and factory purposes.

THE AMERICAN DRUG MANUFACTURERS' ASSOCIATION ENDORSES THE COÖPERATIVE PUBLICITY PLAN OF THE A. PH. A.—At the annual meeting of this Association held at the Biltmore Hotel, New York, April 13, the following resolution of indorsement was adopted:

*Resolved*, That the American Drug Manufacturers' Association endorse the plan of the Federation Committee of the American Pharmaceutical Association for coöperative publicity in American Pharmacy as set forth in the six enumerated propositions in the Committee's report for 1918 through 1919, and that the President be and is hereby instructed to appoint a Committee on Publicity of three members whose chairman shall sit on the National Committee on Pharmaceutical Publicity. And be it further

*Resolved*, That the Committee on Publicity be authorized to extend a sum not exceeding \$200 per annum.

The coöperative publicity plan endorsed by the preceding resolution is as follows:

1. Each national association invited to send delegates to the Federation Conference held in Chicago last year (1918), be requested to appoint a committee on publicity and the chairman of each committee thus chosen or some other representative of the particular organization shall constitute a national committee on pharmaceutical publicity, to which shall be added as an ex-officio member the editor of the *Journal of the American Pharmaceutical Association*.

2. Certain pages of each issue of the *A. Ph. A. Journal* (not to exceed six at first) shall be set aside for the reproduction of matter furnished by members of the national committee on publicity; said matter consisting of journal editorials, abstracts of papers and news items that are of interest to the public.

3. All such material described in Section 2 shall be sent to the editor of the *Journal of the A. Ph. A.* at least ten copies of each

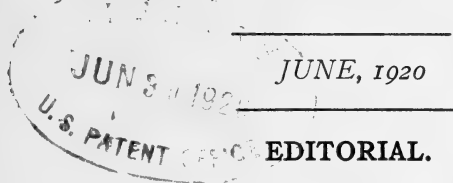
such articles being furnished by the contributor. It shall be the duty of the editor of the *A. Ph. A. Journal* to submit each article to each member of the national publicity committee, and if one negative vote is recorded such article will not be published.

4. All approved articles which have been published on the special pages of the *A. Ph. A. Journal* described in Section 2 will be sent as soon as possible after publication in the *Journal* as reprints preferably in sheet form, to a selected list of newspapers and magazines; the list of such publications being compiled by a sub-committee of the national committee on pharmaceutical publicity.

5. The expense of printing, reprinting and mailing reprints to magazines and newspapers shall be apportioned among the several organizations represented on the national committee of pharmaceutical publicity, upon such basis as the committee and its participating associations shall decide.

6. In addition to the publicity method outlined in Sections 2, 3, 4 and 5, the committee shall be empowered to arrange for the publication of special original articles bearing on pharmacy, in popular journals of large circulation; details for such methods of publicity being left to the proposed national committee.

# THE AMERICAN JOURNAL OF PHARMACY



## THE SIXTY-EIGHTH ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

The 1920 meeting of the American Pharmaceutical Association, held in the New Willard Hotel, in Washington, May 6 to May 10, is now an event of the past. The Capitol city, always beautiful, looked at its best with the bright foliage of the full spring time enriching the landscape view. With ideal weather and an attentive local committee under the able chairmanship of Samuel L. Hilton, determined to make every one enjoy himself or herself to the utmost, another memorable cycle in the history of American pharmacy was completed. The space at our command will not permit of a recount of much that occurred and so we can only here record some of the occurrences that impressed themselves upon the writer as the high spots of the convention.

Wednesday, May 5, the day immediately preceding the opening of the A. Ph. A. meeting, was devoted to meetings of the collateral associations, the National Association of Boards of Pharmacy and the American Conference of Pharmaceutical Faculties. Probably the most important action considered by the latter body was the recognition of the fact that two years for the instruction in the course for pharmacy students, as outlined by the Syllabus, was totally inadequate. The conclusion arrived at was that commencing with 1925 this should be lengthened to a three-year course of instruction. Thoughtful pharmacists long ago realized that a sound professional superstructure, the pharmaceutical education now necessary, could not be erected, even with the improved foundation assured, in two years of collegiate instruction. It appears to us as a rather anomalous position that this conference, many of whose leading

members have been so vociferous in proclaiming for higher professional pharmacy, should have been so slow in recognizing the necessity for a more thorough collegiate education as a basis for professional status and still more strange that having come to such a realization that a public acknowledgment was required, they should still persist in delaying for five more years a reform that should be inaugurated at once. The arguments used as a justification for this postponement are not at all consistent with the ideals that have been professed.

The first general session of the American Pharmaceutical Association was opened on Thursday, May 6, at 3 P.M., in the small ballroom on the tenth floor, and without unnecessary formalities. Local Secretary Hilton announced that the policy of the American Pharmaceutical Association was to receive the credentials of the delegates from the Government Departments and from other Associations and to refer these to the House of Delegates and in the meetings of this House these delegates would have the privilege of presenting whatever messages they had to convey.

President L. E. Sayre called Vice-President T. J. Bradley to the chair and read his presidential address. In this the various topics that are at this time demanding consideration of pharmacy and several internal problems of the Association were discussed in a manner that demonstrated that the President had deliberated on these and had a clear conception of their importance and had arrived at a definite conclusion on a number of them.

The efforts of the A. Ph. A. to interest veterans of the World War in the work of the Association through the medium of an "Advisory Committee" and later the creation of a War Veterans' Section was recounted. His reference to the centennary of the U. S. Pharmacopoeia and the discussion of the vexing question of what should be included in the U. S. P. and the N. F., was thoughtful and consistent and the conclusions quoted such as we can endorse as to the best interests of the professions which these volumes serve.

"As long as medicine is both a science and an art, and so long as clinical therapeutics is able to produce results by the use of remedial agents whose worth cannot be demonstrated by the pharmacodynamic experiment, we will be forced to admit drugs and preparations of both classes. To do otherwise would be tantamount to destroying the work of centuries of experience and dogmatically asserting the value of scientific method which has not yet been able

fully to prove itself. No one will claim that the present scope and content of the U. S. P. is perfect and beyond reproach. A certain amount of judicious "pruning" must be done with each successive revision. Even the ardent conservatists do not believe in keeping worthless material in an official volume. They do, however, most emphatically insist that until there is proof positive, not alone by the methods of experimental pharmacology, but also by the bedside experience, that a drug is worthless, that it be recognized and standardized as are those of more evident potency.

"If we should agree to limit as useful drugs and preparations those only that give visible results in the pharmacological laboratory, and recognize for standardization only these, I am convinced we should be guilty of unfair treatment to the art of medical practice.

"Until medicine and pharmacy shall become more exact sciences than they are to-day, there will always be plenty of room for a difference of opinion as to what is valuable and what is not among the remedial agents which are now recognized; what is worthy of recognition in the United States Pharmacopoeia and National Formulary and what shall be excluded as unworthy of such recognition from these volumes. The policy of admission into these national publications has been very largely based upon what is generally accepted as remedial in character by the medical profession as a whole; not by the few, but the many, who find occasion for their use. What is thus regarded as useful by the many, it is believed, should be standardized as far as pharmaceutical and medical science may accomplish this end. It is interesting to note here how doctors disagree as to what is and what is not useful. A prominent physician made to me the significant remark: 'As long as clinical data and laboratory findings are at such variance it is unwise to be opinionated on the point of drug values.' It should always be borne in mind that U. S. P. and N. F. recognition does not carry with it a favorable recommendation. The U. S. P. and N. F. are not to be considered as treatises on therapeutics, but that they have the same relation to medicine as the United States publications containing certain standards for foods have to the public. What the public uses as foods is included in the U. S. standard for them. It must be admitted that a certain kind of prestige is given to a remedial agent when it is admitted into either the U. S. P. or N. F., but if one mistakes this kind of prestige for a recommendation the fault lies with one's power of discrimination."

The treatment of the subject of prohibition and the duty of pharmacy under the Congressional enactment for its enforcement is in full accord with the editorial position on this subject assumed by the AMERICAN JOURNAL OF PHARMACY.

"Pharmacists, and revisers of our national standards for drugs, have been brought face to face with problems connected with the administration of the prohibition law. This law, aside from its strictly moral phase, is an expression of the decent element of society irrespective of party against intemperance and the saloon. One of our English writers has said that, speaking from a European point of view, one of the curious things about the adoption of prohibition in the United States, extremely characteristic of the American temperament, is the good-natured way in which it was accepted. Men who were not prohibitionists, many who had drunk all their lives and believed that liquor was necessary for their well-being, have made willing sacrifice. Whether this critic understands the American psychology or not, the liquor interests are practically out of business. This is a condition, not a theory, the public faces, whether good-naturedly or not. As to the pharmacists, they have as a class been advocates of prohibition, and they very naturally resent, after being recognized by the Government as legal custodians of medicinal alcoholic liquids (including medicinal liquors), being classified as *retail liquor dealers*. It is worthy to note in passing that the Volstead Act is a distinct recognition of the pharmacist as a proper dispenser of medicine and that the dispensing of alcoholic liquors can be controlled through the profession of pharmacy. Since the Volstead Act recognizes the sale of distilled spirits and wines for medicinal purposes and other prescribed non-beverages and places upon the pharmacist alone the responsibility of dispensing them for medicinal use, the contention may fairly be held that, the sale of intoxicating liquors for beverage purposes being no longer lawful, to license a pharmacist as a liquor dealer as now prescribed by statute makes him appear to be a violator of the purpose and intent of the prohibitory law; this is unjust. If the Government wishes to recognize as a public need the sale of spirits and wines for medicinal purposes and places this task (and it will be a task) on the pharmacist, it should not begin by prejudicing the public against the pharmacist by designating him as a vender of the very articles the sale of which the country has specifically chosen to prohibit.

"Council letters presenting the situation indicate that a protest

should be made—one that will doubtless meet the hearty approval of this Association and one that will result probably in the elimination of the objectionable title. We are told that an Act of Congress would be necessary to change the classification. Doubtless our Congressmen will appreciate the fairness and justness of this protest and it is to be hoped that our Association, at this time, will provide proper measures, through the Council, to bring about a relief to pharmacists from the odium which this unfortunate classification brings. By headlines and articles, by what should be considered as unwarranted reflections upon the profession, sensation mongers, in exploiting their trade, are doing much to make this odium more difficult for the professional pharmacist to bear. It may be said, in this connection, that one of the prominent members of the Council believes that the pharmacist should be entirely relieved of dispensing of liquor and the Government should be asked to assume the sole responsibility of dispensing it. It is the opinion of your president that the dispensing of medicines is a duty properly belonging to the pharmacist. So long as those liquors, the sale of which has been prohibited except as medicine, are regarded as remedial agents, it would certainly be an evasion of responsibility to decline to perform this service of dispensing. If any pharmacist degrades himself and his calling by illegally dispensing these medicinal agents, he should be held responsible and prosecuted the same as if he wilfully violated the narcotic law.

“As unpleasant and unfortunate as it may appear, should we not be true now to the duty placed upon us, and in the meantime may we not, by constant and persistent research, reduce the use of liquors in every way feasible and endeavor to find a proper and adequate non-habit producing substitute for them? Here is a field of investigation worthy of the coöperation of the pharmaceutical and medical professions.”

Among the topics of internal interest to the Association was the question of the *Journal of the American Pharmaceutical Association* and the various suggestions that had been offered for changing the scope and improving the *Journal* and for increasing the activities of the the Association by increasing the income from dues. It may be said in passing, later it was determined that at least some of these questions will be submitted to the membership in a referendum vote to be taken by mail.

The question of pharmaceutical research has been one of the

uppermost topics for several years and this not only occupied attention through the presidential reference to the subject but cropped out in the report of the Committee on Research and also in the discussions in the sessions of the Association and of its Council.

The President's estimate of the Council and its work and especially that of the Executive Committee of the Council which merited his approval is in marked contrast with some of the criticisms that have been made of the actions and recommendations emanating from the St. Louis meeting of this Committee held during the year.

Following the reading of the President's address the Nominating Committee was appointed and again discharged its duty in the same way that has been so frequently criticized and which by a majority vote the members present at a later meeting determined to continue.

An adjourned meeting was held on Thursday evening preceding the President's reception. An address was delivered by Dr. C. E. McClung, representing the Division of Medical Sciences of the National Research Council. The speaker detailed the methods that had been adopted for the organization of this Research Council and the distribution of the millions of dollars that had been subscribed for promulgating scientific researches. It was only too apparent to his audience that the possibilities of pharmacy as one of the most important fields for research for the benefit of mankind had not been given proper consideration.

Happily, Prof. J. U. Lloyd was called upon to respond to Dr. McClung and in his inimitable manner he very cleverly pointed out the inexhaustible fields from which pharmacy draws her stores; how every portion of the globe, every natural kingdom, the air and earth and its mines, as well as the animals and vegetation that thrived thereon, supplied the remedial agents employed by the pharmacist and the unlimited fields for investigation for the advancement of science and the sum of human knowledge to the benefit of mankind was opened through pharmaceutical research in the special fields that the researches spoken of as contemplated did not cover.

Despite the fact that but eight months had elapsed since the prior meeting was held in New York, there was no lack of papers and each section was able to arrange an interesting program. In recent years the Section on Commercial Interests has forged ahead with addresses on timely subjects by leading authorities and this again was in evidence at the Washington meeting. On Saturday morning,



Mr. Merle Thorpe, the editor of the *Nation's Business*, the magazine published by the Chamber of Commerce of the United States, delivered a most enlightening discourse upon the ethics of business. Taking as his title, "Business is Business," his audience was treated with a presentation of the modern methods of the model man of commerce and a view of the expanding field of commercial enterprise and export trade in various lines open to the industries of the United States. He closed his discourse by reading a poem to Spring, whose serio-comic lines filled his audience with visions of the happy days when they were "filled with Juniper and Sassafras" and left them convulsed with mirth and enjoyable delight.

Prohibition Commissioner John F. Kramer then addressed the meeting on the subject of the work of the prohibition enforcement division. The prohibition of the liquor traffic for beverage purposes was not only a radical but also a very sudden change in the policy of this Nation and the work of organizing a governmental department to enforce the legislation enacted was a gigantic task, a big job for any man, but they were going to get away with it. The progress already made was satisfactory and the attitude of the people of this country showed that prohibition was here to stay. He expressed his sympathy with pharmacists upon whom the Volstead Act had placed greater responsibilities as the sole dealers in alcoholic liquors at retail. He was of the opinion that the liquor dealer as a handler of beverage spirits was a thing of the past and that the treasury laws and regulations should be modified so that the title of "Retail Liquor Dealer" would not be retained for the pharmacist who was granted a permit under the Enforcement Act to use and sell non-beverage spirits for medicinal purposes.

He expressed himself as gratified as to the attitude of helpful cooperation with his department that had been shown by representative men in pharmacy and the drug trade organizations and appealed for universal assistance from the druggists as the class of men whose interests were the most affected by prohibition legislation.

Immediately following Commissioner Kramer, Mr. William L. Crounse, Attorney for the National Wholesale Druggists' Association, read a carefully prepared paper on "Alcohol—Its Importance in Science and Industry." In this the writer declared that alcohol was the most essential chemical raw material known to science. He criticized the attitude of the prohibition zealot and the ignorance of this class who were continuously guilty of gross misrepresentation

of the necessary uses of alcohol as a basic material in pharmacy and the chemical industries. His comments upon the work of the Bureau of Internal Revenue should be viewed as constructive criticism of value to the officials thereof. His review of the divided opinion among pharmacists themselves as to the proper attitude that they should assume regarding the dispensing of liquors on prescription, was a very fair presentation of an unfortunate difference. This address, we hope to publish in full in the next number of the JOURNAL.

One of the most encouraging signs of the time, was the changed attitude of the Governmental Departments concerning pharmacy. On the opening day of the meeting of the A. Ph. A., a committee composed of members of the Committee on Status of Pharmacists in the Government Service, had very pleasant interviews with Secretary of the Navy Daniels, Admiral Thos. Washington, head of the Bureau of Navigation, U. S. N., Surgeon General Braisted, of the Navy and Surgeon General Ireland of the U. S. Army. The spirit pervading was in marked contrast to that of a few years ago when it was officially declared "that pharmacists were not essential to the Army." Not only were the medical departments of the Army and Navy represented by officers officially appointed by the respective surgeon generals who attended the meetings of the Association and in the House of Delegates presented the greetings of their commanding officers and expressed the desire of their departments for the assistance of pharmacists and the aid of representatives of the profession in organizing and improving the medical service insofar as it related to pharmacy. Moreover, Surgeon General Braisted of the Navy, who was likewise President of the American Medical Association, welcomed the opportunity for making a personal address to the Association.

The Committee on Nominations submitted the following names for President, 1921-1922: Henry Kraemer, Ann Arbor, Mich.; Charles W. Johnson, of Seattle, Wash.; Samuel L. Hilton, Washington, D. C. The election will be by means of a mail ballot.

The Council later elected as the Honorary-President for this year John F. Hancock, of Baltimore, Md. The Council was re-organized with Prof. Charles H. LaWall as chairman, and Dr. A. G. DuMez as secretary. It was decided to hold the next meeting in New Orleans in September, 1921.

G. M. B.

## THE PHARMACOPOEIAL CONVENTION.

On Tuesday morning, May 11, the delegates composing the United States Pharmacopoeial Convention for the Tenth Revision of the U. S. P., assembled in the ballroom of the New Willard Hotel in Washington. Shortly after 10 A.M., the appointed hour, the President, Dr. Harvey W. Wiley, called the convention to order and the business of the assemblage was proceeded with in a most expeditious manner. Beyond the appointment of delegates from the several departments of the government service represented, official Washington took no cognizance of an important gathering of professional and scientific experts for the explicit purpose of performing a most valuable service to the American people, the preparation of the standards for the most commonly dispensed medicines and which by the laws of Congress and many of the States, become the official standards of the country for drugs.

The report of the Committee on Credentials was read by Secretary M. G. Motter and showed no contests and required only a few corrections. It exhibited, however, a pathetic ambition on the part of some pharmacists to be admitted as delegates to this convention. Proxies and credentials from distant organizations, by some agency, found their way to persons who were recorded as delegates of such bodies with which prior to this perambulation they had not the slightest acquaintance and with which they were in no way whatever associated.

President Wiley called Fifth Vice-President Dr. W. A. Bastedo to the chair and read his presidential address which on motion was referred to a committee for consideration and report at the subsequent meeting. This was followed by the reports of the chairman of the Board of Trustees, Secretary and Treasurer of the convention, the latter showing a very comfortable balance available for the expenses of the convention and revision.

The report of Chairman LaWall for the Committee of Revision was read and this, and, likewise, the President's address contained touching references to the services of the late Chairman Remington and tributes to his work. On motion the president appointed Dr. S. Solis-Cohen, Charles H. LaWall and George M. Beringer as a committee to prepare a minute expressing the sentiments of this convention on the decease of Chairman Remington. In connection with his report Chairman LaWall read a paper prepared by E.

Fullerton Cook on "The Machinery of the Pharmacopoeial Revision," containing a number of suggestions for the expediting of the revision. The convention referred these to the incoming revision committee. (The report of Chairman LaWall appears in this number of the *AMERICAN JOURNAL OF PHARMACY* and the paper of Prof. E. Fullerton Cook, embodying the suggestions made to the convention, was published last month.)

The several amendments to the Constitution and By-Laws recommended by the Board of Trustees and which had been published in advance in the medical and pharmaceutical journals, were adopted as offered.

The Committee on Nominations was then selected, each delegation, as the organization was called by the Secretary, naming its representative thereon, and the meeting adjourned till Wednesday morning.

At the second session, held on Wednesday A.M., the Committee on President's Address made its report recommending that this be published and given a wide distribution. The committee to draft an appropriate minute concerning the decease of Chairman Remington submitted the following, which was adopted by a rising vote in silence.

"The Pharmacopoeial Convention assembled for the tenth decennial revision, deeply mourns that Professor Joseph P. Remington, Chairman of the Committee of Revision, who bore the brunt and burden of the labor of the revision was called from this life on January 1, 1918, before this body could express its appreciation for his painstaking efforts in the eighth and ninth revisions, by which the scientific standing of the volume was advanced and its leading position in the pharmacopoeias of the world established. No man can have a nobler monument than has Joseph P. Remington in this work.

"This Convention records its deep sense of the loss which the pharmacopoeia and the professions whose interests this work serves, sustained in his demise, and their obligation for the unselfish service, the many sacrifices, and the devotion to the pharmacopoeia continuously manifested throughout his many years of association with the work of the revision.

"This assemblage attests its esteem for his character, its love for his personality, its admiration for his learning and extends to his

family its sincere sympathy in their bereavement in which it likewise claims to share.

"As a lasting tribute to his memory and recognition of his inestimable service this minute is entered upon the records of this Convention and a copy thereof transmitted to his family."

The Nominating Committee made a report recommending the following for the respective officers:

For President, Dr. Reid Hunt.

For First Vice-President, Dr. Frederick B. Power.

For Second Vice-President, Dr. M. Howard Fussell.

For Third Vice-President, Dr. Walter A. Bastedo.

For Fourth Vice-President, Prof. L. E. Sayre.

For Fifth Vice-President, Dr. John F. Anderson.

For Secretary, Dr. L. F. Kebler.

For Assistant Secretary, Dr. W. W. Stockberger.

For Treasurer, Samuel L. Hilton.

For Trustees, James H. Beal, F. J. Wulling, Henry M. Whelpley, Dr. George H. Simmons, Dr. S. Solis-Cohen.

For members of the Committee of Revision to be composed of fifty, the names of seventeen physicians and thirty-three pharmacists and chemists were presented.

This report was adopted without division and in record-breaking time. The report on General Principles To Be followed in Revising the Pharmacopoeia submitted by the retiring committee was taken up and considered seriatim. A few minor changes in the wording were made without effecting any material alterations in the principles proposed and the twenty-six propositions each under a distinct title were adopted as a whole for the guidance of the incoming Committee on Revision.

Having discharged its work expeditiously the convention was adjourned *sine die* at the end of this second session.

The new Committee of Revision was called together on Thursday afternoon, May 12, by the President, Dr. Reid Hunt, for the purpose of effecting its organization. Dr. H. V. Army nominated Prof. E. Fullerton Cook for chairman and he was unanimously elected. Prof. W. L. Scoville was elected Vice-Chairman and Prof. Charles H. LaWall was made Secretary. The committee immediately got down to work and held two meetings before adjournment at midnight and, by adopting the suggestions that had been made by Prof. Cook, accomplished in these conferences the division of its membership

into sub-committees, each of which selected its chairman who becomes thus a member of the Executive Committee, and settled by discussion a number of mooted questions which heretofore have required several months spent in correspondence for determination.

As we reflect upon the events of the Pharmacopoeial Convention and the machinations preceding, we are fully aware that these evidence the need for some reform in the methods adopted for the appointment of delegates to the convention and likewise for the selection of the officers and committee of revision. The recommendations of Chairman LaWall were unquestionably correct and efficiency alone should be the guide in determining the selection of those upon whom these important duties are to devolve. We cannot, however, record that they made a very deep impression upon many of those present, despite caucus agreements and conventional endorsement. The peripatetic efforts of certain over-ambitious and radical elements allied to pharmacy were fraught with grave danger to the future of the Pharmacopoeia. Fortunately, a measure of sound judgment prevailed so that with providential guidance a fairly representative committee of revision was selected. We can but regret that the wire-pulling of the educational elements resulted in the naming of so few practical pharmacists on the committee and yet this book is the constant and direct guide of this class of users who outnumber ten-fold that of any other class.

We would draw the veil of charity over the acts of jealousy that blinded from the observation of some of the delegates the efficient, self-sacrificing services of others in behalf of the pharmacopoeia and the elevation of the practice of pharmacy. G. M. B.

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## THE TAX ON TOILET ARTICLES AND PROPRIETARY MEDICINES.

To avoid apparent confusion in the minds of the public regarding the collection of the tax on toilet articles and proprietary medicines, the Bureau of Internal Revenue has issued a statement advising both dealers and purchasers that the tax of 1 cent for each 25 cents or fraction thereof of the amount paid is on the article itself and not on the total amount paid by the customer when two or more such articles are purchased, unless of the same kind and put up by the manufacturer in a single container for sale as an original package.

For example, if a tube of tooth paste costs 35 cents and a bottle of perfume 65 cents, the tax is 2 cents on the tooth paste and 3 cents on the perfume, a total of 5 cents and not 4 cents as computed on the total amount paid by the purchaser.

If toilet powder sells at 10 cents a box, the tax is one cent; if two boxes are bought the tax is two cents, although the total amount paid by the purchaser is 20 cents; and if three boxes are bought for 25 cents, the tax is 3 cents. If however, six boxes of toilet powder selling singly at 10 cents each are put up by the manufacturer in a container or sealed package for sale as a unit and are sold by the dealer as an original package for 50 cents, the tax is 2 cents, the package being the unit of sale.

The regulation providing that where two or more packages of cough drops are sold for 25 cents the tax shall be 1 cent is revoked, the tax being at the rate of 1 cent for each 25 cents or fraction thereof of the amount paid for a single package.

Instructions to advise dealers that the tax shall be collected in accordance with this ruling have been sent to collectors of internal revenue. The public is requested to cooperate in the proper collection of the tax.

This new ruling clarifies and to some extent, likewise, modifies prior announcements from the Bureau of Internal Revenue on this subject. We believe that it is entirely in harmony with the intent of the section of the Revenue Law of 1918 relating to this form of luxury tax. We are constrained, however, to direct the attention of the Bureau to the fact that the ruling of the Department relating to the tax to be collected upon multiple sales of ice cream, soda water, coca cola, etc., is inconsistent with this decision concerning the collection of the tax under the same law on multiple sales of toilet articles and proprietary medicines.

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#### FRANK G. RYAN.

On the afternoon of April 20, Frank G. Ryan, president of Parke, Davis & Co., died rather suddenly of a malignant attack of pneumonia after an illness of but three days. Funeral services were held at Christ Church, in Detroit, on April 22. The active pall bearers were those who had been closely associated with him in the business management and a group of about fifty of the prominent representatives of the business and professional life of Detroit, all personal

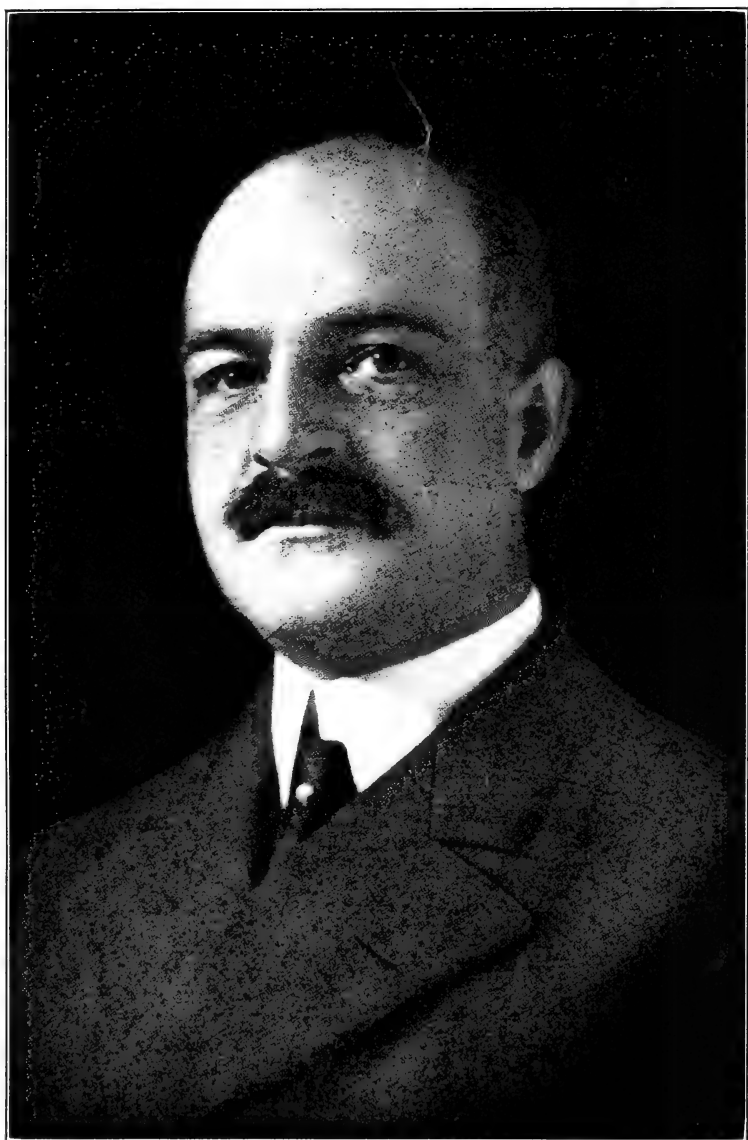
friends, comprised the honorary pall bearers. The church was filled with a sorrowing throng composed of all walks in life, as Mr. Ryan had endeared himself to each whether a humble workman or girl employee in the office or laboratory, or a prominent professional or financial leader of the city and they all joined in paying a last tribute to one who was so universally esteemed.

Frank Gibbs Ryan was born in Marcellus Falls, New York, on December 26, 1861. He was educated in the public schools of Elmira. At the age of fifteen, he engaged in the drug business. During the years 1880-1882 he was employed as a drug clerk with Brown & Dawson, pharmacists, of Syracuse, the junior member of which firm was secretary of the New York State Board of Pharmacy for a number of years.

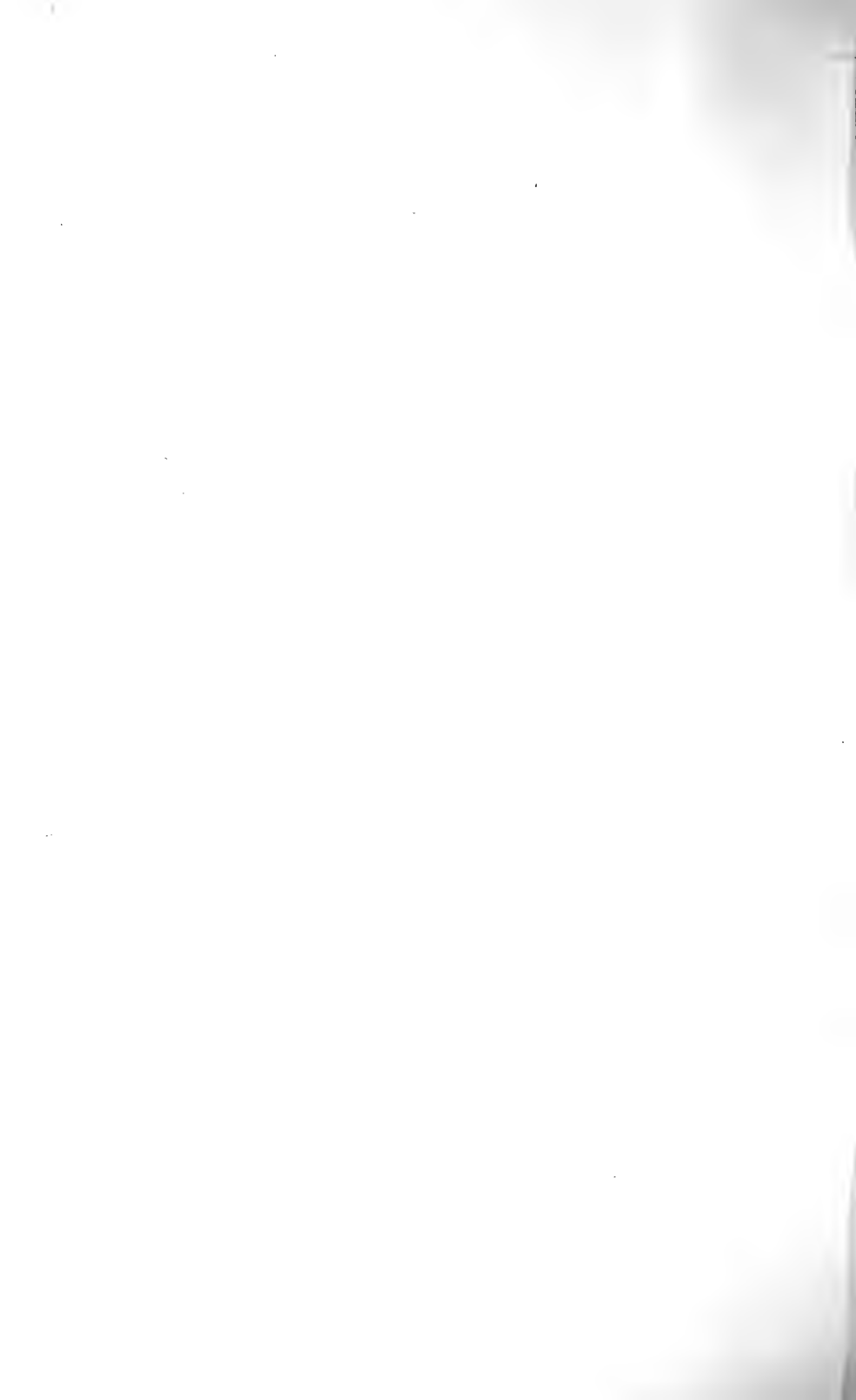
In 1882, Frank came to Philadelphia and matriculated at the Philadelphia College of Pharmacy. While attending instruction at the college, he clerked in several stores in Philadelphia and for several years after completing his college course he continued to keep in close touch with the actual duties of the retail pharmacist. Nevertheless, it was apparent even then, that he was gathering a broader experience as a teacher and as a student of commercial methods that would serve as a foundation for higher attainments. In 1884, he was graduated from the Philadelphia College of Pharmacy, the subject of his thesis being "*Magnesii Carbonas.*"

In 1887, he was selected by Prof. Joseph P. Remington as his assistant in the department of Pharmacy. Both the professor and assistant Ryan were convinced that the instruction in pharmacy must be broadened out and much more attention be given to the commercial or business training of the embryo pharmacists, and that it was a proper part of the work of the College to see that the student was well-grounded in the essentials of business knowledge as well as in the professional and theoretical part of his calling so that the danger of an unsuccessful career would be minimized. It was largely through the efforts of Frank G. Ryan that in 1899 the College decided to establish an optional course in commercial training and this branch of instruction was placed in his charge. This was an entirely new departure in the curricula of pharmaceutical schools and attracted considerable attention and comment. Within a few years, the value of the instruction was demonstrated and was incorporated as part of the established curriculum of the Philadelphia College of Pharmacy and it has since been added to the instruction





*Frank G. Ryan*



given in many other schools of pharmacy. To Prof. Frank G. Ryan belongs the honor of having been the pioneer in this branch of pharmaceutical education and despite the early criticism he lived to see his ideas and the very course of instruction that he had outlined made the basis for the accepted course of business training in the leading schools of pharmacy.

At the meeting of the American Pharmaceutical Association held in Richmond, in 1900, Prof. Ryan was requested to address the members upon the subject of commercial training for students of colleges of pharmacy. He said that the lack of business knowledge on the part of the young men engaging in the drug business had been discussed in the pharmaceutical journals and was undoubtedly real. In his experience he found that but one man in twenty had received any training in business principles, although his students were generally high school graduates and possessed a good general education.

As clerks the young men had little opportunity to learn about the market conditions, the correct methods of buying, discounts, banking and insurance, etc., as this part of the business was almost universally reserved for the proprietor. The business colleges were prepared to teach a man how to become a banker, broker, shipper, real estate dealer but none of these taught business methods as applied to the buying and selling of drugs specifically, and it was essential that the pharmacist should receive such before engaging in business on his own account and this should be imparted as part of his collegiate training and preferably by those who had some acquaintances with drugs and the drug-trade customs. He submitted a synopsis of what he considered as the essentials that should be included in this instruction.

In 1889, when the scope of his duties in the Philadelphia College of Pharmacy were widened and the instruction in commercial training added, he was given the title of Instructor in Pharmacy and Assistant Director of the Pharmaceutical Laboratory. At the same time, he held the position of lecturer on pharmacy in the Woman's Medical College of Philadelphia. Always courteous, yet forceful, he evidenced even in those early days that he was a born leader of men and that he possessed unusual administrative and executive ability that enabled him to command and to gain the respect, confidence and support of students and the development of these characteristics at that time and under circumstances that were

trying to say the least, doubtless had an important bearing upon his subsequent success.

Affluence may have been a dream of this ambitious young pharmacist but at that period of his career it was an unknown factor. One of his classmates recently narrated that on the Commencement night when Ryan was awarded the pharmacy prize of \$25.00 he remarked to his friend that this was a fortunate relief from being "flat broke." Intelligent and industrious application of his time was, however, a fundamental principle and for some years the summer months, when his college duties were for the time being suspended and which a less ambitious teacher would have enjoyed as a deserved vacation, found him engaged with Parke, Davis & Co. as a representative in attendance at conventions and in detailing physicians. He thus gained further experience and invaluable information and insight into human nature especially as reflected by those following the medical profession.

In 1900 he determined to relinquish teaching as his calling in life and cast his lot with manufacturing pharmacy and accepted the position of head pharmacist with Parke, Davis & Co. After thirteen years' connection with the instructional work of his *Alma Mater* he resigned in May of that year and the Trustees very reluctantly accepted his resignation and he carried with him the sincere best wishes of the officers, members and faculty and it has been with justifiable pride that they have since marked his great success. The severance of the many ties of comradeship and association with innumerable friends in the east must have caused him some "heart pangs" as it did those he was leaving.

We now know that this change meant at the time not only the taking up of a new and to some extent an unknown activity but that it likewise entailed a financial sacrifice as the initial salary was less than he was making by his several activities in Philadelphia.

With his characteristic self reliance and determination he applied himself to the enlarged field of opportunity. For three years he was one of the executive heads of a department energetically applying himself to learning every detail of the business and applying the knowledge which he had gained by his scientific and commercial training. When the opportunity came for filling vacancies in advanced positions of trust and responsibility his commanding position was so evident that he was invariably chosen. His advancement was phenomenal and to those unacquainted with the man and his ability,

both innate and acquired, would have been considered as romantic. In less than seven years, from the time that he permanently cast his lot with this corporation, he had been elected first, a Director, then, Secretary, next, Vice-President and, finally, President. The latter position he filled for thirteen years when the Divine call terminated his labors. The thirteenth year would thus again appear as the completion of a determining cycle in his career.

As vice-president of Parke, Davis & Co., Mr. Ryan made a tour around the world combining pleasure with business. While in London, in 1907, he was entertained at a public dinner by the leading pharmacists and prominent men connected with the drug trade. Returning to America, he had landed but a day when President Buhl was suddenly stricken and Frank G. Ryan was immediately elected to fill the highest office in the Company. As president for the intervening period he accomplished great things for this house and the perfected organization, the enormous developments along scientific as well as commercial lines are very largely attributed by his associates to his foresight and ability and to the inspiration of his character and policies.

Frank G. Ryan joined the American Pharmaceutical Association in 1892. He was immediately elected secretary of the Section on Scientific Papers for the year and in 1899-1900 was chairman of this Section. He served as Chairman of the Committee on Weights and Measures and made an excellent report of the bills that had been introduced into Congress favoring the general adoption of the Metric System. He was not an office seeker and was contented to give his advice and the weight of his influence for the betterment of pharmacy without receiving personal recognition. Such offices and honors that were accepted came unsolicited and as a recognition of merit. He took an active interest in the organization and work of the American Drug Manufacturers' Association and for the first two years of its existence served as its President and the success and achievements of this comparatively young, yet exceedingly active, organization again demonstrates and reflects the effect and influence of the master mind in its formative period.

He filled an important position in the civic life of the City of Detroit. He was a member of five of the leading clubs of the city and served a term as president of the Detroit Club and of the Country Club. He declined to accept a number of public duties that were proffered to him. Nevertheless, he was an intense student of

the economic and political events of the time. His advice was freely sought on many subjects and his judgment and opinions were greatly esteemed. During the war, the governmental authorities frequently sought his advice on matters relating to the drug trade and he also served as chairman of a local draft board and gave unstintedly of his time and energies in this service.

A close friend of Mr. Ryan has written "he was preëminently a man who carved out his own career from the hard rock of opportunity. He rose from the ranks of drug clerks to a position of commanding influence in the pharmaceutical world." As we study the life work of those who have achieved notable successes, we find it interesting to isolate the personal characteristics that were the determining factors in their elevation. The personal traits that dominated the life and determined the preëminence of the subject of this sketch are not difficult to be discerned. Among these we may mention quickness of perception, promptness of decision, intense earnestness, unquestioned justness, sympathetic nature, unswerving integrity, close application, confidence in himself coupled with unusual administrative ability and adamant adherence to principles. These were the qualifications that enabled him to inspire others with enthusiasm and the development of their best efforts, that won for him the respect and admiration of his business associates and competitors and endeared him to a host of friends.

His decease came with alarming suddenness and was a great shock to the community and the wide circle of friends. He left his office on Saturday, April 17, apparently in good health. That night he was taken with a severe chill and the next morning medical attendance was called in and the ailment was promptly diagnosed as a dangerous type of pneumonia from which he succumbed on Tuesday afternoon, less than three days after being taken ill. He is survived by a daughter, Mrs. Charles A. Dean, Jr., of Detroit, and a grandson, Charles A. Dean, 3rd, in whom Mr. Ryan was especially delighted.

G. M. B.

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## REPORT OF THE CHAIRMAN OF THE COMMITTEE OF REVISION OF THE U. S. PHARMACOPOEIA.

BY CHARLES H. LAWALL, PH.M.

In presenting the report which the by-laws of this organization direct shall be made to the Decennial Convention by the Chairman

of the Revision Committee, I must remind you that the real report, the one to which the Convention is entitled, written by the Chairman of the Committee who occupied that important post during the active period of revision, can never be presented. He who has borne the burden and heat of the day has been taken from us, and I, who was so close to him in his work for so many years, realize more than ever the loss that American pharmacy has sustained, and that no surrogate can stand before you and do justice to such a task or perform it in the manner in which it would have been handled by our late Chairman Remington.

In my hands the report will necessarily be limited to a chronological record of major events in the decade just ending. It will lack the fire and enthusiasm which would characterize a report by the one who was Chairman for a period of nearly seventeen years. This period (from 1901 to 1918) was the most important in the history of this ancient and honorable book of standards, for there is only one other national pharmacopoeia in existence which is older than the United States Pharmacopoeia and none which is more important; it is the period which saw the United States Pharmacopoeia emerge from a position of interest only to a limited number of practicing physicians and pharmacists who were bound by the ethics of their respective professions to heed its mandates, to the supreme position which it now occupies as the book of standards recognized as authoritative by both national and state governments in the laws pertaining to drugs.

At the decennial meeting of the Convention in May, 1910, a change was made in the former plan of having a Revision Committee of twenty-five, a larger committee of fifty members being selected. This included the following:

Joseph P. Remington,	C. Lewis Diehl,
William C. Alpers,	George C. Diekman,
John F. Anderson,	A. R. L. Dohme,
H. V. Arny,	E. G. Eberle,
E. H. Bartley,	C. W. Edmunds,
George M. Beringer,	Joseph W. England,
Wilhelm Bodemann,	J. M. Francis,
Charles Caspari, Jr.,	J. M. Good,
C. E. Caspari,	H. M. Gordin,
Virgil Coblentz,	W. G. Gregory,
N. S. Davis,	Walter S. Haines,

C. S. N. Hallberg,  
R. A. Hatcher,  
Lewis C. Hopp,  
Reid Hunt,  
L. F. Kebler,  
J. A. Koch,  
Henry Kraemer,  
Edward Kremers,  
Charles H. LaWall,  
J. H. Long,  
A. B. Lyons,  
Philip Marvel,  
C. F. Nixon,  
O. T. Osborne,  
Albert Plaut,

W. A. Puckner,  
Otto Raubenheimer,  
George D. Rosengarten,  
H. H. Rusby,  
S. P. Sadtler,  
L. E. Sayre,  
J. O. Schlotterbeck,  
Torald Sollmann,  
A. B. Stevens,  
R. H. True,  
C. E. Vanderkleed,  
M. I. Wilbert,  
H. C. Wood, Jr.,  
H. W. Wiley.

This Committee immediately held an organization meeting before leaving Washington and elected the following officers:

<i>Chairman,</i>	Joseph P. Remington.
<i>1st Vice-Chairman,</i>	C. Lewis Diehl.
<i>2nd Vice-Chairman,</i>	H. C. Wood, Jr.
<i>Secretary,</i>	Charles H. LaWall.

The Committee then dispersed and under the guidance of its newly elected officers, three of whom lived in Philadelphia, commenced organizing by mail for the formation of the Executive Committee of Revision of fifteen members, which had been authorized by the changed by-laws. Before this organization had progressed materially, Dr. Edward Kremers resigned from the Committee and his place was filled by the election of Dr. Solomon Solis-Cohen. The Executive Committee, as finally selected by the group of members interested in these respective lines of work, was as follows. The names of those who served upon these various sub-committees are also given as a matter of record:

No.	Title.	Chairman.	Members.
I	Scope (Admissions and Deletions)	S. Solis Cohen	Cohen, Dohme, Hallberg, Hunt, Marvel, Osborne, Plaut, Rusby, Sollmann, Wood



No.	Title.	Chairman.	Members.
2	<i>Therapeutics and Pharmacodynamics</i>	Torald Sollmann	Cohen, Davis, Edmunds, Haines, Hatcher, Osborne, Sollmann, Wood
3	<i>Biological Products, Diagnostic Tests</i>	J. F. Anderson	Anderson, Hatcher, Hunt, Long, Sollmann, Edmunds, Wood
4	<i>Botany and Pharmacognosy</i>	Henry Kraemer	Kebler, Kraemer, Plaut, Rusby, Sayre, Schlotterbeck, True
5	<i>General and Inorganic Chemistry</i>	C. H. La Wall	Army, Bartley, C. E. Caspari, Coblenz, Kebler, La Wall, Long, Puckner, Rosengarten, Sadtler
6	<i>Organic Chemistry</i>	G. D. Rosengarten	C. E. Caspari, Coblenz, Dohme, Kebler, Koch, LaWall, Lyons, Puckner, Rosengarten, Sadtler, Vanderkleed
7	<i>Proximate Assays</i>	A. B. Stevens	C. E. Caspari, Dohme, Francis, Gordin, Kebler, Kock, La Wall, Lyons, Puckner, Stevens, Vanderkleed
8	<i>Volatile Oils</i>	H. W. Wiley	Beringer, C. E. Caspari, Dohme, Francis, Koch, LaWall, Sadtler, Kebler, Wiley
9	<i>Fluid and Solid Extracts, Tinctures</i>	G. M. Beringer	Beringer, Chas. Caspari, Jr., Diehl, Diekman, Francis, Eberle, Good, Raubenheimer
10	<i>Aromatic Waters, Spirits, Liquors</i>	C. Lewis Diehl	Army, Beringer, Bodemann, Diehl, Eberle, England, Good, Gregory, Raubenheimer

No.	Title.	Chairman.	Members.
11	<i>Syrups and Elixirs</i>	W. C. Alpers	Alpers, Beringer, Diehl, Diekman, Eberle, England, Francis, Nixon
12	<i>Cerates and Ointments</i>	Otto Raubenheimer	Alpers, Diekman, Eberle, England, Good, Hopp, Raubenheimer
13	<i>Miscellaneous Galenicals</i>	C. S. N. Hallberg	Arny, Bodemann, Hall- berg, Hopp, Nixon, Raubenheimer, Sayre, Wilbert
14	<i>Tables, Weights, Measures</i>	A. B. Lyons	Kebler, La Wall, Lyons, Stevens, Wilbert
15	<i>Nomenclature</i>	Chas. Caspari, Jr.	Caspari, Jr., Cohen, Good, Hallberg, Os- borne, Plaut, Rusby, Wilbert

On October 22, 1910, death removed Prof. C. S. N. Hallberg, Chairman of the Sub-committee No. 13. His place upon the Executive Committee was immediately filled by the selection of Mr. Wilhelm Bodemann, and the vacancy in the General Committee of Revision was filled by the election of Prof. A. H. Clark, on January 7, 1911.

No other deaths occurred in the Executive Committee during the active period of the work of revision, which lasted until the summer of 1916. The work of the General Committee and of the various sub-committees was mainly carried on by correspondence. One fairly representative personal conference participated in by a majority of the members of the General Committee of Revision was held during the meeting of the American Pharmaceutical Association in Boston, Massachusetts, on August 15, 1911. Several official and numerous unofficial meetings were held of important sub-committees during the active period of work, but in the main the entire operation of revision was conducted by the method in use during the preceding decade—that of mimeographed circulars and letters and a definite procedure of debating questions and collecting and recording votes.

We can form some idea of the magnitude of this stupendous undertaking when we glance at the statistics of the work as expressed in pages of material issued during the decade, most of which was sent out prior to 1916.

Circulars to General Committee	2000 pages (9 × 16 inches)
Letters to Executive Committee	3417 pages (8½ × 11 inches)
Bulletins to members of Sub-committees from the chairmen (members of the Executive Committee)	5557 pages (8½ × 11 inches)

These latter figures are underestimated, for no record is obtainable for three of the sub-committees, and no account whatever is taken of the voluminous personal correspondence which was carried on by or between members throughout the entire progress of the work.

The first task to be accomplished was the selection of the substances for inclusion in the revised work. This duty was assigned to the Sub-committee on Scope, which made five preliminary reports from December 8th, 1910, to March 11th, 1911. Some changes were subsequently made as new conditions arose necessitating modification or alteration of previous action. When the book finally appeared, however, the sum total of changes in monographs amounted to sixty-seven additions and two hundred and forty-three deletions. There are seven hundred and eighty-two titles and monographs included in the official substances in Part I. In Part II there are three hundred and thirty-nine test solutions and reagents described and a number of special descriptive articles covering general processes or subjects, together with numerous tables of value.

In the progress of the work, the following procedure was followed in the main. A tentative monograph was submitted to the sub-committee to which that particular substance had been assigned, by its chairman, and comments and suggestions invited. The chairman of the sub-committee would then draft a new monograph embodying the changes suggested and again submit it to the members of the sub-committee. This procedure was repeated until a monograph was found to satisfy the members of the sub-committee. During this stage of the work, the chairmen of the sub-committees who were members of the Executive Committee, reported monthly to the Chairman of the General Committee of Revision upon the status of the work in their respective sub-committees. When a group of monographs satisfactory to a sub-committee had been collected by its chairman, these were submitted to the Executive Committee through the General Chairman and comments and suggestions invited. Sometimes the monographs with their criticisms would be

resubmitted to the committee from whence they had come, but more often the corrections were of a minor character and the monographs would be finally revised by the Executive Committee. Having passed this group of censors, the revised or approved monographs would next be sent out to the General Committee of Revision, where they were subjected to the scrutiny and criticism of many who had not before seen them. Again the procedure of correcting minor errors or recommitting was followed and the monograph, having reached this advanced stage and having been finally approved, was put aside by the Chairman of the General Committee of Revision, until the entire manuscript was ready for the printer.

During the Executive Committee and General Committee stages of the evolution of these texts, the mandate of the Convention regarding publicity was heeded, by submitting to the numerous pharmaceutical, medical and chemical journals lists of all proposed changes in abstract. These proposed changes were also widely circulated among the manufacturing firms of the country, thus calling in as an auxiliary a great body of interested and experienced scientific workers who performed services of great value without adding to the cost of the work.

One of the burning questions occupying the attention of the members of the Revision Committee themselves, and interfering to a certain extent with the efficiency of their work through pressure from the outside, was the query: How long is the revision going to take? Such a factor should never enter into a problem of this kind. For several decades each succeeding revision has taken a little longer than the last, for the reasons which are clearly apparent to a rational unprejudiced observer. Under the present methods of procedure, in which practically all of the work is carried on by mail in the interests of economy, it may always be expected that a revision will require from three to six years. When the Convention wishes a more expeditious handling of the work, it can easily obtain results by authorizing a large enough expenditure of funds to enable personal conferences to take the place of long drawn out arguments and discussions by correspondence and in the interest of scientific efficiency by authorizing the establishment of a central laboratory where all scientific problems can be worked out, at least in a preliminary way, without having to wait for the convenience of those who are doing the work largely as a labor of love and with

a generous sacrifice of time and energy usually transferred from more remunerative work.

The most unthinking criticism in connection with pharmacopoeial revision is usually directed at this matter of time taken to revise the work. It generally originates in quarters where unfamiliarity with the problem is the principal asset of the critic. So far as any specific reasons may be given for the long period consumed in the revision of the U. S. P. IX, it may be stated primarily that this was the first complete revision of the work after the passage of the Food and Drugs Act, giving it authoritative legal standing, and, in consequence of this fact, every standard, every phrase, had for the first time in the history of a revision to be so carefully framed as to afford no loop hole for evasion by, or escape of an adulterator on the ground of indefiniteness. American lawyers must be extraordinarily keen or most be more in the habit of interposing technical objections or raising technical points of interpretation than are the lawyers of other countries, for forms and procedures which appear to be perfectly practical in the pharmacopoeias of many other nations were objected to, criticised and revised until our present United States Pharmacopoeia seems to some to be overbalanced in the direction of academic preciseness and to have lost something of the spontaneity and practicality of some of the earlier editions. This may all be necessary and unavoidable, but the present Convention and the incoming Committee of Revision should not lose sight of the fact after all that the United States Pharmacopoeia should be a practical guide-book first and a law-book next. The European war, which began just as the revision was nearing completion, brought new problems to be solved and new difficulties to confront the revisers, and this influence was also of a nature to retard the progress of the work.

Some questions consumed much time in discussing and were finally decided adversely, so far as admission was concerned. Among these were the following:

The inclusion of a table of antidotes.

The introduction of a standard medicine dropper.

The publication of ethical rules for guidance of physicians and pharmacists in their relation to each other and to the public.

The admission of whisky and brandy.

The rules of procedure entitle every member to a reasonable

length of time to formulate his arguments in a discussion and the question is then decided by a majority of the votes of the entire Committee either for or against the proposition. In this connection it may be said that the present procedure leaves much to be desired as it works out in practice in many instances, especially when questions come to a vote in the General Committee. It is not uncommon in such a case, when the vote is tabulated, to find that those who may rightfully claim to be experts on a particular subject and who have given time, thought and study to a subject in addition to experience which they possess, are outvoted by members who are not particularly familiar with the question except in so far as they have been informed by the discussions which they have read. This defect has persisted for several revisions, and attention was called to it by late Chairman Remington in his report to the last Decennial Convention. I feel it necessary at this point to quote his remarks upon this subject verbatim:

"The Pharmacopoeia is a composite work and one of the defects in the last revision was the fact that the whole committee were expected to vote upon questions of detail, the vote of each member having the same value. This should be changed, and, upon special subjects, the sub-committee having these in charge should have much greater weight in the final decision than heretofore. This can be done by referring, for example, assay subjects, which have been before the General Committee, back to the sub-committee, if necessary, and each member of that committee might have two votes on the final decision, the same rule to apply to all sub-committees.

"Another way of meeting this difficulty would be to allow any member of the General Committee, not especially posted upon matters of detail, to transfer his right to vote to a member of the sub-committee in whom he has confidence. This vital defect in pharmacopoeial revision might then be overcome."

I believe it would be well for the Convention this time to give some very careful thought to this subject and to issue binding instructions to the incoming Committee covering this very important phase of the work. For example, it certainly is exclusively the province of the medical members of the Revision Committee to decide what substances should be officially included for remedial purposes, and this list, after having been decided upon by the physicians, should not be subject to review or alteration by pharmacists and chemists. On the other hand, when the list of official remedial

agents has once been clearly outlined, it should be the province and privilege of the pharmacists and chemists to decide upon such additions and inclusions of materials used as ingredients as will make it possible and practicable to prepare the medicine of proper uniformity, quality and potency. These are the basic and fundamental prerogatives, and a workable plan should be devised to maintain their integrity.

The work of making a pharmacopoeia is big enough and important enough to enlist the constructive effort of every worker, be he physician, pharmacist or chemist, and by having a clear understanding of the respective responsibilities and duties and an intelligent allotment of the details of the work much lost motion may be saved and a unanimity of effort developed which will not only expedite the progress of the work, but will develop a common interest of thought and action between physicians, pharmacists and chemists who are co-laborers in the important field of work which has for its ultimate object the alleviation of human suffering and the prevention and cure of disease.

In the early part of 1916, the preliminary work of revision was practically finished. The manuscript was placed in the hands of the printer and the great task of editing, proof reading and finally correcting the copy, proceeded rapidly to completion. Galley proofs were sent to the members of the Executive Committee and page proofs to all members of the General Committee of Revision, the majority of whom co-operated splendidly in this important labor. Comments and corrections were systematically compiled by the General Chairman and carefully considered in preparing the final page proof. Foundry proofs were sent only to the General Chairman. The work was at last completed in the summer of 1916 and the time of making the U. S. P. IX official was fixed for September 1st of that year.

It has been stated and it is undoubtedly true that insufficient time was given from the time when the books were actually available in the furthestmost parts of the great geographic territory to which the United States Pharmacopoeia applies and the date when the work became official. Six months is not too long a time for the interests involved to make the necessary changes in labels and stocks and to minimize the confusion always attendant upon such a period of change. The Convention should adopt a definite resolution upon this point.

No work of such magnitude has ever yet been free from error or just criticism. It is gratifying to report, therefore, that when an official list of corrections and necessary changes was issued in 1919, three years after the work had become official, only 101 alterations were reported, a small number indeed, and most of them were of minor importance.

On January 1, 1918, Chairman Remington died at his home in Philadelphia. He was immediately succeeded by the 2nd Vice-Chairman, Dr. Horatio C. Wood, Jr., the 1st Vice-Chairman having died some time previous.

Following the procedure of the previous decade when a similar situation occurred, Dr. Wood called for an election for Chairman of the General Committee of Revision, and upon April 6, 1918, I, Charles H. LaWall, was elected to fill the vacancy for the remainder of the ten-year period of office.

Death had fortunately spared the Committee during the early and constructive period of the work, only one death having occurred prior to 1915, that of Prof. C. S. N. Hallberg, previously referred to. The other deaths which occurred during the decade were as follows:

Mr. Albert Plaut,	June 17, 1915.
Mr. M. I. Wilbert,	November 25, 1916.
Dr. W. C. Alpers,	February 20, 1917.
Prof. C. Lewis Diehl,	March 25, 1917.
Dr. J. O. Schlotterbeck,	June 1, 1917.
Prof. Charles Caspari, Jr.,	October 13, 1917.
Dr. John H. Long,	June 14, 1918.
Prof. James M. Good,	May 15, 1919.

From this it will be seen that out of the fifty-one members of the General Committee of revision ten, or 20 per cent., died during the decennial period for which they had been elected.

Early in the summer of 1918 an election was called for to fill the vacancies occasioned by death up to that time. Nominations were made of candidates and, after balloting, the following eight members were elected:

Prof. E. Fullerton Cook,	Mr. J. K. Lilly,
Prof. W. B. Day,	Dr. L. G. Rowntree,
Mr. S. L. Hilton,	Mr. L. A. Seltzer,
Mr. H. P. Hynson,	Prof. W. J. Teeters.



On September 27, 1918, Prof. E. F. Cook was elected Secretary of the General Committee of Revision to fill the place made vacant by the election of myself to the general chairmanship. Vacancies having occurred in the Executive Committee by death and other causes, the following chairmen were elected during 1918 of the sub-committees named:

- No. 5 Dr. H. V. Army.  
 10 Prof. E. G. Eberle.  
 11 Mr. J. W. England.  
 15 Dr. H. H. Rusby.

At the present time, therefore, the entire personnel of the sub-committees, with assignments of newly elected members is as follows:

No.	Title.	Chairman.	Members.
1	<i>Scope (Admissions and Deletions)</i>	S. Solis-Cohen	Cohen, Dohme, Hunt, Marvel, Osborne, Rusby, Sollmann, Wood, Hynson
2	<i>Therapeutics and Pharmacodynamics</i>	Torald Sollmann	Cohen, Davis, Edmunds, Haines, Hatcher, Osborne, Sollmann, Wood
3	<i>Biological Products, Diagonostical Tests</i>	J. F. Anderson	Anderson, Hatcher, Hunt, Edmunds, Sollmann, Wood
4	<i>Botany and Pharmacognosy</i>	Henry Kraemer	Kebler, Kraemer, Rusby, Sayre, True, Day, Lilly, Tecters
5	<i>General and Inorganic Chemistry</i>	H. V. Army	Army, Bartley, C. E. Caspari, Coblenz, Kebler, Puckner, Rosengarten, Sadtler, Clark
6	<i>Organic Chemistry</i>	G. D. Rosengarten	C. E. Caspari, Coblenz, Dohme, Kebler, Koch, Lyons, Puckner, Rosengarten, Sadtler, Clark, Vanderkleed
7	<i>Proximate Assays</i>	A. B. Stevens	C. E. Caspari, Dohme, Francis, Gordin, Kebler, Koch, Lyons, Puckner, Stevens, Vanderkleed, Hilton

No.	Title.	Chairman.	Members.
8	<i>Volatile Oils</i>	H. W. Wiley	Beringer, C. E. Caspari, Dohme, Francis, Koch, Sadtler, Kebler, Wiley
9	<i>Fluid and Solid Extracts, Tinctures</i>	G. M. Beringer	Beringer, Diekman, Francis, Eberle, Raubenheimer, Cook, Hilton
10	<i>Aromatic Waters, Spirits, Liquors</i>	E. G. Eberle	Army, Beringer, Bodemann, Eberle, England, Gregory, Raubenheimer, Cook, Hilton, Hynson, Seltzer
11	<i>Syrups and Elixirs</i>	J. W. England	Beringer, Diekman, Eberle, England, Francis, Nixon, Cook, Hilton, Hynson, Seltzer
12	<i>Cerates and Ointments</i>	Otto Raubenheimer	Diekman, Eberle, England, Hopp, Raubenheimer, Cook, Hilton, Hynson, Seltzer
13	<i>Miscellaneous Galenicals</i>	Wilhelm Bodemann	Army, Bodemann, Clark, Hopp, Nixon, Raubenheimer, Sayre, Cook, Hilton, Hynson, Seltzer, Teeters
14	<i>Tables, Weights, Measures</i>	A. B. Lyons	Kebler, Lyons, Stevens
15	<i>Nomenclature</i>	H. H. Rusby	Cohen, Osborne, Rusby

In 1918 the Board of Trustees authorized the publication of a supplement to include some new remedies and some of the changes made advisable by the continuance of the war and the shortage of supplies. The sudden end of the war eliminated the immediate necessity for a supplement, and it being near the end of the revision period, the Board of Trustees withdrew the authorization which they had previously made for its publication.

The Spanish Translation which had been authorized by the Convention was placed in the hands of the printers during 1918 and in December, 1919, was placed on sale through the same agency which had handled the previous Spanish Edition, they being the lowest bidders for the privilege. The publication of the Spanish Edition can never be considered financially advantageous to the Convention, but it should be continued as a patriotic duty and in recognition of the increasing use of the book in the Spanish speaking American countries.

The last work of the Committee has been to draft a set of General Principles for submission to the Convention, embodying the experience and constructive thought of the present Committee. These will be submitted for your consideration and discussion at the proper time. There have also been collected a large number of suggestions and criticisms for the guidance of the incoming committee in planning and carrying on its work. All of those which came in before January 31st, 1920, have been collected, classified and published in the *Journal of the American Pharmacuetical Association* and reprints are now available for distribution and will be turned over to the incoming committee.

Much material of the same kind which has accumulated since will be made a part of the records of the present committee. These records will also include the final reports and recommendations of a few of the sub-committees which are still functioning, and all of this material will be available for immediate use by the newly elected Committee of Revision.

The plan of subdividing the work into fifteen different headings has worked out well in practice. It would be in the interest of efficiency if in naming the men who are to serve upon the Revision Committee in the next decade that some classification of their qualifications be insisted upon in making the nominations in order that a well-balanced committee might be selected embodying experts in all lines of work. This could be accomplished by instructing the nominating committee to require each nominee to be classified by placing after his name the number of the present U. S. P. sub-committee in which his services would be particularly valuable. By following such a plan, we would be assured of a Committee of Revision to undertake the important work of the next decade, which would be well balanced in character and free from criticism.

I, therefore, recommend that the Convention instruct the nominating committee to proceed upon such lines in carrying out its work.

If the Convention wishes to assure the issuing of the next revision of the Pharmacopoeia within a reasonable length of time, say two years from now, this result can be undoubtedly achieved by issuing instructions to the incoming Board of Trustees and Revision Committee that frequent personal conferences of sub-committee members be authorized and periodic meetings of the Executive Committee of Revision. This is tendered as a suggestion rather than as a recommendation.

To this assembled Convention is submitted the foregoing report of the work of a Committee which, as far as its present personnel is concerned, ceases to exist officially within the next few hours. There is no greater honor or responsibility than can come to a physician, pharmacist or chemist than of being included in this galaxy of workers. What the present Committee has accomplished has been done under the stimulus of the high standard set by the previous revision, of which so many commendable things were said by foreign critics, who may be expected to have a broader perspective and a fairer viewpoint in some respects than those who are close at hand. Many of our members have labored in season and out to make the book worthy of American medicine and pharmacy. Whether we have succeeded or not, it is the best that was possible to be done under existing circumstances. The time, thought, energy, we may even say the life-blood of men who did the best they knew how, are woven into its structure.

To this Convention is entrusted the responsibility of selecting the next Revision Committee. Whatever be the conditions under which the next revision will be undertaken, you should not lose sight of the fact that capability and willingness to serve are the fundamental considerations that should guide you in your choice. There should be an entire absence of rivalry or jealousy except that which animates men who are each trying to see who can best work and best agree. The next United States Pharmacopoeia should be a work which will enlist the support of that which is best in the professions sharing the responsibility of its revision.

The initials are symbolic of three guiding principles which should be kept ever in mind, for without them no true success can be achieved. They are Unity, Service and Patience, and in closing let me again say that revisions may come and go, but it will be long before you will find a chairman who will exemplify these attributes as did Chairman Joseph P. Remington, whose memory might suitably be honored at this time by selecting men of his unselfish, loyal and steadfast type to revise the next United States Pharmacopoeia.

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## CALCIUM CARBONATE IN PHARMACY AND MEDICINE.

By ADLEY B. NICHOLS, Phar.D.,

PHILADELPHIA, PA.

Chalk, chemically mainly calcium carbonate, is the name given to any soft, pulverulent, pure white limestone. The word chalk is an old one, having its origin in the Saxon "cealc," and the hard form "kalk" is still in use in some districts. The German word "Kalk" comprehends all forms of limestone, and therefore a special term "Kreide" is employed, French "Craie."

Chalk is used extensively in a great many ways. It enters into the manufacture of cement and other commercial articles; it finds a place in various chemical processes, and in the making of paint, crayons and tooth powders. Whiting, or Spanish white, which is used to polish glass and metal, is purified chalk, prepared by elutriation. Chalk is employed to some extent medicinally, sometimes as a mild astringent, but more usually for its mechanical action as in grey powder, or in chalk mixture where it produces its effect by coating the walls of the stomach and intestines.

At the present time, most of the calcium carbonate used in medicine is obtained from natural deposits, of which there are a few in the United States, while the largest deposits, in the form of whole mountain ranges, with huge white chalky cliffs, are found in southern England and extending directly across the channel and through northern France. This natural chalk is called *creta alba*.

Calcium carbonate is official in two different forms in the present U. S. Pharmacopœia, as *Calcii Carbonas Praecipitatus*, so-called precipitated chalk, and as *Creta Praeparata*, so-called prepared chalk. The precipitated article is prepared by interaction between calcium chloride and sodium carbonate, calcium carbonate being precipitated. This differs physically from prepared chalk, which is native chalk prepared by elutriation, in that the particles are more gritty and it is not usually so near white in color, and also lacks the adhesive qualities which are so pronounced in prepared chalk. The precipitated chalk is better adapted for use in tooth powders, and similar preparations, on account of its gritty character, while the prepared chalk is used extensively in medicine as an antacid, besides being particularly well adapted for the treatment of diarrhoea, by reason of its adhesive properties.

The method for preparing precipitated chalk was first made official in the fourth edition, 1850, of the U. S. Pharmacopœia, while the prepared chalk was official in the first and second editions, as *Calcis Carbonas Praeparatus*, and the title changed to the present form of *Creta Praeparata* in the third edition, 1840. Likewise *Mistura Calcis Carbonatis* was official in the first two editions of the Pharmacopœia, and was changed to *Mistura Creta* in the third edition. The U. S. Dispensatory, first edition, 1833, also added, that besides being official in its soft state, as chalk, carbonate of lime is also ordered as it exists in marble (*marmor*), oyster shells, crabs eyes and crabs stones. The preparation called *Testa Praeparata*, was recognized in the U. S. Pharmacopœia from the first to the sixth editions inclusive. *Testa* is the term applied to the shell of the oyster, *Ostrea Edulis*, L., consisting of about eighty-seven to ninety-eight per cent. of calcium carbonate and found mostly in the internal pearly layer of the shell. *Conchae* was another term used to designate oyster shells, prepared by boiling with water and freed from all foreign matter, and *Conchae Praeparatae*, the purified oyster shell, purified by elutriation and trochiscation.

At the present time there is a preparation of this type official in the Homoeopathic Pharmacopœia, by the name of *Calcarea Carbonica*, or Calcium Carbonate of Hahnemann, and is sometimes known as *Calcarea Ostrearum*, or *Testa Ostryae*. This is impure carbonate of lime as it exists in the oyster shell, and is directed to be prepared as follows: Take well selected, tolerably thick oyster shells, clean and break in a wedgewood or porcelain mortar. Select the pure white portions which exist between the interior and exterior surfaces, wash carefully in distilled water, dry over a water bath and reduce to a fine powder.

According to theories accepted at that time, *testa* was supposed to be more acceptable to the stomach than ordinary chalk. Lewis' *Materia Medica*, 1784, states that lime water dissolves the human calculus, particularly lime water prepared from calcined oyster shells, which proves a more active menstruum for this concrete (and possibly other substances) than that prepared from stone limes, the dissolving power of oyster shell lime water seeming to be more than double that of stone lime water.

There were a great many other drugs, besides oyster shells, which were used at various times as sources of calcium carbonate, and

possibly the next in general use were crabs eyes, or crabs stones, which were known by such terms as *Lapides Cancrorum*, *Lapilli Cancrorum* or *Oculi Cancrorum*, being concretions found in the stomach and consisting of about sixty-four per cent. of calcium carbonate, with a little animal matter. King's Dispensatory gives the following tests to distinguish the true from the spurious crab's eyes. They effervesce in hydrochloric acid in which they do not completely dissolve, thus being distinguished from spurious crab's eyes, which are wholly dissolved by hydrochloric acid. In the presence of boiling water, crab's eyes assume a pinkish red hue. Another closely related product was crab's claws, *Chelae Cancrorum*, which were prepared in a finely powdered state and consisted of about sixty per cent. of calcium carbonate.

Corallen or Coral, was still another of the forms of calcium carbonate used, and this too is still used in the Homoeopathic Pharmacopœia, under the name *Corallium Rubrum*, or red coral, the skeleton of the coral zoöphyte. The chemical constituents are calcium carbonate with a trace of magnesium carbonate and a little more than four per cent. of ferric oxide as coloring matter. There is a small amount of animal matter present. This is also called carail rouge.

Os sepia, or cuttlefish bone, the mantle of *Sepia Officinalis* L., is still another of the many forms of calcium carbonate relied upon. This consists of from eighty to eighty-five per cent. of calcium carbonate. Its use lies mainly in furnishing calcium carbonate to cage birds.

An interesting note on lime water dating back to the nineteenth century, states that lime water was originally prepared from "*calcaria usta*," as lime was called, and the preparation was known as "*Aqua Calcaria Usta*."

Other waters of this nature were mentioned under such names as *aqua calcarea bicarbonica*, aerated or carbonated lime water, and *aqua magnesiae carbonica*. *Aqua* or *liquor magnesiae carbonica* was made either by freshly precipitating magnesium carbonate from magnesium sulphate and sodium carbonate and saturating with carbon dioxide, or using *magnesia alba* directly and then saturating.

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THE STABILITY OF DIGITALIS LEAF EXTRACTS. THE  
INFUSION (SECOND PAPER).

BY CLAYRE A. POMEROY AND FREDERICK W. HEYL,

KALAMAZOO, MICHIGAN.

In a previous paper<sup>1</sup> the deterioration of alcoholic digitalis extracts was discussed and a rather rapid rate of deterioration was established. A study of the stability of aqueous solutions is important because of the wide use of the infusion in practical therapeutics. It is also interesting to observe the behavior of such solutions because of the fact that most of the investigators to whom we owe our present information concerning the chemistry of the leaf have used processes involving the use of aqueous solutions.

Infusion of digitalis is the oldest of the galenical preparations of this drug, and was in fact employed by Withering, to whom we owe the introduction of the drug to modern practice. He began to use it as a diuretic and the dose used is stated as 1-3 grains twice a day or the equivalent amount of infusion (1-3 drachms of 1.5 per cent. infusion).

Aside from the clinical value of the infusion, which it is not our purpose to discuss, our brief investigation points out conclusively that in the modern evolution of pharmacy we have lost some of the unique powers of observation which the pharmacists of the 18th and early part of the 19th century had developed to such a degree that their personal interest could be relied upon in the matter of collecting and selecting drugs. The olden-time pharmacist knew his digitalis and the activity of the infusion. The modern pharmacist must necessarily rely upon the assistance of the pharmacologist in this matter. During the interval between the old period and the time when complete scientific standardization shall be used, such problems as that presented by infusion of digitalis must prove a stumbling block to clinical progress.

We have recently been required to answer a large number of inquiries on the part of clinicians concerning the strength and stability of the infusion. Not only do we find a wide variation in the strength of various samples of leaves, but the instability of the infusion itself lends further variability to this preparation. The pharmacist relies upon indirect sources of supply for his crude drug, and

<sup>1</sup> *Am. J. Pharm.*, 91: 425, 1919.



then manufactures the unassayed infusion, usually in liter quantities as prescribed in the pharmacopœia. He does well if he produces a preparation equal in value to those made in the earlier times when the clinician's report to the pharmacist constituted something of a pharmacological opinion on the drug used.

While it is true that the pharmacopœia wisely directs that the infusion must be freshly prepared from the leaves, the fact is that the quantities outlined in the text, which produce one liter of the preparation, leads most pharmacists in practice to overstock this galenical.

Our results upon the stability of the infusion proved of great interest. When this subject is studied using the one-hour frog method, we find that the infusion stored at low temperatures will lose about 20 per cent. of its activity in 6-7 days; while in warmer weather, the velocity of the change is greater and the same stage of decomposition results in 3-5 days. It would appear reasonable therefore to limit the production of the infusion to small quantities. An excellent system of digitalis administration which is widely used in this country consists in giving 3-8 grains daily for several days until the desired therapeutic effect is obtained, with subsequent diminution to 1-3 grains per day. If we adopt this, it is evident that since one teaspoonful (4 Cc.) of the infusion is equivalent to 1 grain (0.06 Gm.) of the drug that a four ounce (120 Cc.) quantity constitutes a very desirable quantity of the infusion for prescription work. This amount of infusion contains about 31 grains (2.00 Gm.) of the drug and this supplies a quantity usually considered necessary during a 5 to 7-day course.

Our conclusions are based upon the deterioration rate as determined by the one-hour frog method. Hatcher and Eggleston,<sup>1</sup> using the cat method have reported results that lead to the conclusion that "the infusion is fairly stable when prepared and kept with ordinary care, no important change then occurring within a week." They report stability of an order never observed by ourselves. Thus for example, they found an official infusion that had been kept stoppered at 70° F. for 19 days to test the same as at the beginning. In another case, a specimen made by the official process and kept in the ice box for four weeks retained its activity unchanged. An aqueous infusion after 28 days in the ice box retained about 80 per cent. of its activity. It is necessary to refer the reader to the original

<sup>1</sup> J. A. M. A., 65: 1902, 1915.

paper, but their findings are certainly entirely different from those obtained by the one-hour frog method.

Concerning the comparative activity of infusions and tinctures we obtain results similar to the previous findings of Focke.<sup>1</sup> This investigator reports that infusions filtered through linen or cotton give slightly higher results than when filter paper is used. The activity corresponds to about 85 per cent. of that obtained in tinctures of equal concentration. We believe that this figure will represent the average finding when a considerable number of samples are investigated in this connection. Some of our fresher samples yielded almost as much of their activity to water as to the tincture, while in the case of a very old drug only 70 per cent. of the total activity was found in the infusion. For practical purposes Focke's figure is acceptable and the dosage of the infusion should perhaps be slightly higher (10/9) than for the powdered drug. In other words, considering 0.06 Gm. of digitalis (4.0 Cc. infusion) as a standard dose of the powdered leaf, the activity of the infusion will require about 4.4 Cc. to yield the same result.

If one bears in mind the instability of aqueous digitalis solutions, while reviewing some of the chemical studies of the leaf, it becomes easy to comprehend the difficulty of the investigators in arriving at concordant results. Practically all the workers, including Schmiedeberg, Kiliani and Kraft, have worked in aqueous media, and we daresay that, dependent upon conditions, various products have been isolated which represent various degrees of alteration.

In connection with the chemical investigation of the leaf it appears to be important to bear in mind the fact that the total activity of the crude galenical extracts may greatly exceed the sum of the isolated fractions, even if no chemical changes such as hydrolysis were involved. This subject is discussed by Tschirch and Wolter,<sup>2</sup> who reported the interesting observation that the activity of the acetone extract of a salt saturated aqueous solution of digitalis represented but a part of the total activity, whereas the extracted fluid proved to be inactive. Acetone extracts the active principles from the leaf completely. They state that this difference in results is to be understood either by reason of chemical change in the active principles or because in the activity of crude extracts other substances which, while they are not in themselves active,

<sup>1</sup> *Arch. Pharm.*, 249: 323, 1911.

<sup>2</sup> *Schweiz. Apoth. Zeit.*, 56: 469. THIS JOURNAL, 91: 471.

have nevertheless an influence upon the active material. This influence is either in relation to solubility or absorption which is influenced favorably. Tschirch argues that the activity of digitalis is an ensemble effect and is not due to simply the sum of individual glucosides; instead the activity of each individual is always influenced and increased by the simultaneous presence of others. With the successful isolation of individual glucosides the ensemble activity does not appear upon physiological testing.

These investigators performed a simple experiment of interest in this connection and bring out a point which is overlooked in our first paper. Putting the drug through Keller's assay, they isolated 18.5 per cent. of the activity in the chloroform shake out. The exhausted aqueous layer retained only 26 per cent. of the activity, so that by simple exhaustion of the aqueous solution with this inert solvent over half the activity disappears. Loss of activity may be due therefore not only to spontaneous changes, which are described in the experimental part, but also to the destruction of loose native combinations and the loss of the mutual effects found only in the native drug.

#### EXPERIMENTAL.

*A. Some Observations upon the Comparative Activity of Fresh Tinctures and Fresh Infusions of Digitalis Made from the Same Drug.*—Drug (F2190) stocked November 20, 1918. A 10 per cent. tincture assayed 130 per cent. (11-30-18).

Date.	10% Tincture A'. %	10% Infusion (A). %	A/A'.
11-30-18.....	130	...	....
1-14-19.....	135 (F. E.)	...	....
4- 1-19.....	...	130	1.0
10- 1-19.....	110	...	....
9-16-19.....	...	105	0.95
1-15-20.....	...	90	....

From these assays it appears that in extracting this drug during one year the infusions and tinctures were almost equal (within the limits of error of the method).

Another drug was examined on this point (G3316):

Date.	10% Tincture (A'). %	10% Infusion (A). %	A/A'.
1-10-20.....	150	...	....
4-14-20.....	...	120	....
4-19-20.....	140	...	0.86

The infusion in this case represents about 90 per cent. of the total activity of the leaves as represented in the official tincture.

In order to find out whether an aged drug would behave differently we reexamined D1625 on this point. A sample of this lot has been stored since December 5, 1916.

Date.	10% Tincture (A'). %	10% Infusion (A). %	A/A'.
3-1-17.....	135	...	...
4-19-20.....	50	...	...
4-16-20.....	...	35	0.70

From this result it would appear that the activity of the water soluble principles of an old drug represented less of the total activity than in the fresher leaf.

*B. On the Deterioration of 10 Per Cent. Aqueous Infusions.*—The infusion prepared from Drug F2190 was allowed to stand at room temperature (4-1-19).

Time.	Activity, %.	% Deterioration.
At beginning.....	130	0
After 18 hours.....	120	8
After 24 hours.....	120	8
After 48 hours.....	110	15
After 72 hours.....	95	27

This infusion molded on the 3d day, and the work was repeated by filtering a fresh infusion (4-9-19) through porcelain and collecting the filtrate under sterile conditions.

Date.	Time.	Activity, %.	% Deterioration.
4-8-19.....	At beginning	130(?)	...
4-9-19.....	After 18 hours	120	0-8
	After 48 hours	110	8-15
	After 90 hours	100	17-23
	After 144 hours	80	33-38
	After 8 days	76	37-41
	After 11 days	67	44-48
	After 16 days	48	60-63
5-3-19.....	After 25 days	40	66-70
	After 43 days	30	75-77
	After 63 days	30	75
	After 87 days.	27	78

It is thus shown that this elaborately sterilized solution should have been discarded after 3-5 days.

We next proceeded to determine the rate of deterioration when

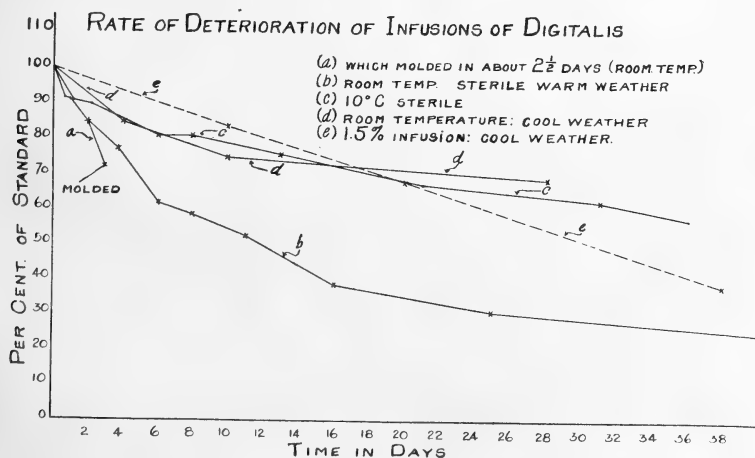
kept in an ice chest at a constant temperature of 10° C. The infusion was prepared and maintained under sterile conditions as above. Drug F2190:

Date.	Time.	Activity, %.	% Deterioration.
9-16-19.....	At once	105	0
	After 30 hours	95	10
	After 54 hours	95	10
9-22-19.....	After 6 days	85	19
9-24-19.....	After 8 days	85	19
9-29-19.....	After 13 days	80	24
10- 8-19.....	After 22 days	70	33
10-18-19.....	After 32 days	65	38
10-23-19.....	After 37 days	60	43
11-10-19.....	After 53 days	55	48
12-17-19.....	After 92 days	45	57
1-26-20.....	After 132 days	40	61

The above work was repeated at room temperature.

Date.	Time.	Activity, %.	% Deterioration.
10-14-19.....	After 24 hours	105	0
10-17-19.....	After 4 days	90	14
10-23-19.....	After 10 days	80	24
11-11-19.....	After 28 days	72	31
12-17-19.....	After 64 days	60	43
1-28-20.....	After 106 days	40	61

Plotting these curves over to 100 per cent. basis as a starting point in each case.



From these curves it is shown that four infusions passed a point of 20 per cent. deterioration as follows:

- (a) Which molded in about  $2\frac{1}{2}$  days.
- (b) At room temperature and warm weather in 3-4 days.
- (c) At  $10^{\circ}$  C. in 8 days.
- (d) At room temperature in cooler weather; 7 days.

*C. Observations on Deterioration of 1.5 Per Cent. Infusion (U. S. P.).*—We purposely began this investigation with 10 per cent. infusions because it was found that in using 1.5 per cent. solutions that considerable concentration was required before injection, *i. e.*, 1.5 per cent. solutions are poorly absorbed. It might be objected that this concentration rather than the storage produced deterioration.

*Expt. I. (1-15-20).*—A fresh 1.5 per cent. infusion U. S. P. was prepared (F2190), and two aliquots of 100 Cc. were concentrated to exactly 15 Cc. thus making the final concentration 10 per cent. One concentration was made upon the steam bath, while the second was concentrated at  $40^{\circ}$  in a vacuum distillation apparatus. Both solutions showed the same activity, *i. e.*, 0.00667 Mil per Gm. frog or 90 per cent. of the standard for the tincture.

*Expt. II.*—Adopting the process of concentration upon the steam bath, we took at intervals 100 Cc. of the sterile 1.5 per cent. infusion and assayed these with the following results:

Date.	Time.	Activity, %.	% Deterioration.
1-16-20.....	At beginning	90	0
1-26-20.....	After 10 days	75	17
2- 6-20.....	After 21 days	60	33
2-24-20.....	After 39 days	35	61

The curve during the first 20 days is exactly like those described for the 10 per cent. infusions "*c*" and "*d*" and it passes the point recording 20 per cent. deterioration at about the 11th day, but we consider the assay upon the 10 per cent. infusion of the fresher drug, which brings this point earlier, as more accurate.

*D. Observations on the Advisability of Adding 10 Per Cent. Alcohol.*—In the U. S. P. of 1890, infusion digitalis is made with the addition of 10 per cent. alcohol. It is true that the addition of alcohol clarifies the solution, and tends to prevent turbidity, but the better appearance tends to delude the pharmacist to accept an inaccurate belief that the stability is thereby increased. The following will

indicate that the addition of 10 per cent. alcohol is without favorable influence upon the stability.

A 1.5 per cent. infusion (10 per cent. alcohol) was examined with the following results:

Date.	Time.	Activity, %.	% Deterioration.
4-14-20.....	3 hours	105	0
4-15-20.....	27 hours	85	19
4-16-20.....	51 hours	65	38
4-17-20.....	75 hours	55	48

#### SUMMARY.

1. A comparison of the relative activity of digitalis infusions and tinctures of equal concentration shows that there is a difference, the infusion being slightly less active.

2. The infusions deteriorate.

3. Placing a 20 per cent. limit on deterioration: The infusions should be discarded in 3-5 days' time. At lower temperatures this time limit may be extended to 6-7 days.

4. The addition of alcohol adds nothing to the stability of the infusion.

RESEARCH LABORATORY,  
THE UPJOHN COMPANY,  
KALAMAZOO, MICHIGAN, MAY 1, 1920.

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### CALCIUM.\*

#### COMPARISON OF TEN DIFFERENT METHODS OF ESTIMATION.

BY GEORGE E. ÉWE.

*Standard Material.*—Practically white, doubly refractive calcite.

*Preparation of Standard Material for Analysis.*—The calcite was ground to a fine powder in an agate mortar, dried to constant weight in a platinum dish over a flame which was not permitted to touch the dish. The dried calcite was free from caustic as shown by its failure to turn red litmus paper when 1 Gm. was made into a paste with a little water and tested with litmus paper. The dried calcite was preserved in a glass stoppered weighing bottle.

*Impurities in the Standard Calcite.*—The usual impurities of calcite are silica, ferric, aluminum, magnesium and manganese compounds.

\* From *Bulletin of the International Metallurgical and Chemical Society.*

The standard calcite yielded the following proportions of these impurities:

SiO <sub>2</sub> .....	0.0119	
	0.0123	Av., 0.0121 per cent.
Fe <sub>2</sub> O <sub>3</sub> -Al <sub>2</sub> O <sub>3</sub> .....	0.01319	
	0.01360	Av., 0.0134 per cent.
MgO.....	None	
Manganese.....	None	

#### SILICA.

A 0.5 Gm. sample was weighed in a platinum dish, a very little water was added followed by 5 Cc. hydrochloric acid (1 : 1). The mixture was evaporated to dryness and the residue baked at 200° C. until free from the odor of the acid; 20 Cc. of 1 : 1 hydrochloric acid was then added and the mixture boiled for about 10 minutes; 30 Cc. water was added; the mixture was boiled and the silica collected on a filter and washed well with hot water. The filtrate was put through the same procedure again but only an unweighable amount of silica was obtained. The filter containing the silica was ignited to constant weight over a blast lamp and weighed; the weight of the silica being corrected for the ash of the filter.

#### FERRIC AND ALUMINUM OXIDES.

The filtrate from the silica was made alkaline with freshly distilled ammonia, only a slight excess of ammonia being used; a few drops of bromine water was added and the mixture boiled until only a very faint odor of ammonia was perceptible. The oxides were filtered off, redissolved in hot dilute nitric acid and reprecipitated with ammonia as before; they were then filtered off, washed thoroughly with hot water and ignited over the blast a short time to constant weight. The weight of the combined oxides was then corrected for the filter ash.

#### MAGNESIA.

The filtrate from the ferric and aluminum oxides was rendered alkaline with ammonia, boiled and 20 Cc. of boiling saturated solution of ammonium oxalate added. The mixture was boiled for five minutes and allowed to settle. The calcium oxalate was filtered off and washed with hot water several times, redissolved in dilute hydrochloric acid and reprecipitated as before. The filtrates from the two precipitations of calcium oxalate were acidified and evaporated to about 150 Cc.; cooled and treated with 17 Cc. of 28 per cent.



ammonia water, followed by 15 Cc. of a 10 per cent. sodium phosphate solution. The solution was stirred well and allowed to stand over night. No weighable amount of precipitate could be obtained.

#### MANGANESE.

Volhard's reaction (a solution of 0.5 Gm. of the calcite in 5 Cc. conct. nitric acid was boiled with an excess of lead peroxide, then diluted with 25 Cc. of water and the insoluble matter allowed to settle), yielded no trace of violet-red color, therefore it was concluded that no more than a negligible proportion of manganese was present, if any.

#### THEORETICAL $\text{CaCO}_3$ CONTENT OF STANDARD MATERIAL.

No evidence was obtained as to how the  $\text{Fe}_2\text{O}_3$  and  $\text{Al}_2\text{O}_3$  were combined in the calcite but it was arbitrarily taken that the two oxides were present in equal proportions and combined as carbonates in the "ic" state, since the proportions were too small to exert any but a negligible influence on the calcium determinations.

Likewise the state of combination of the  $\text{SiO}_2$  was not determined, and while it may have been present in some form of combination with calcium, yet the amount concerned would be negligible, and as a consequence the  $\text{SiO}_2$  was arbitrarily considered as being present in the free state.

The proportion of silica ( $\text{SiO}_2$ ) was..... 0.0121 per cent.

The proportion of  $\text{Fe}_2\text{O}_3$  plus  $\text{Al}_2\text{O}_3$  was 0.0134 per cent., which,

figured to the carbonate state, amounted to..... 0.0286 per cent.

The total of impurities, therefore, was..... 0.0407 per cent.

The difference between this figure (0.0407 per cent.) and 100 per cent. was considered to represent the  $\text{CaCO}_3$  content of the standard material. Thus, the  $\text{CaCO}_3$  content was theoretically 99.959 per cent.

#### DETAILS OF THE DIFFERENT METHODS OF ESTIMATION OF CALCIUM.

No. 1. Precipitating as calcium oxalate and weighing as calcium carbonate.

A 0.5 Gm. sample was freed from silica and iron and aluminum by the methods mentioned under "Methods of Determining Impurities." The calcium was precipitated as oxalate as mentioned under "Methods of Determining Impurities," except that it was washed more thoroughly. The calcium oxalate was dried on the filter,

ignited in a platinum crucible separate from the filter, to a faint redness for 15 minutes in order to convert all of the oxalate to carbonate. This ignition may result in the formation of a little calcium oxide, so, after weighing, the contents of the crucible were moistened with water and a small lump of ammonium carbonate added; the ammonium carbonate was driven off by heating the crucible on a water bath and the crucible then ignited to a very faint redness. This treatment was repeated until constant weight was obtained and the contents of the crucible no longer turned red litmus paper.

Results..... No. 1—99.64  
2—99.49 Av., 99.57 per cent.  $\text{CaCO}_3$

No. 2. Precipitating as calcium carbonate and weighing as such.

A 0.5 Gm. sample was freed from silica and iron and aluminum oxides by the methods outlined under "Methods of Determining Impurities." The filtrate from the iron and aluminum oxides was treated with a little ammonia water and then ammonium carbonate solution in slight excess was added. The precipitated calcium carbonate was allowed to settle for several hours on the top of a covered hot water bath; it was then filtered off and washed with water containing a little ammonia; dried and ignited separate from the filter and weighed as calcium carbonate as described under Method No. 1.

Results..... No. 1—100.05  
2—100.10 Av., 100.07 per cent.

No. 3. Liberating  $\text{CO}_2$  by means of hydrochloric acid and weighing the liberated  $\text{CO}_2$  in KOH solution.

The calcite was placed in an Erlenmeyer containing a three hole rubber stopper. Through one of the holes a glass tube was placed. This glass tube extended to the bottom of the Erlenmeyer. The other end of the tube was connected with several potash bulbs to prevent access of the  $\text{CO}_2$  of the air into the Erlenmeyer. The second hole of the rubber stopper contained a glass tube which reached just below the stopper. The other end of the tube was connected first with a calcium chloride tube, then with a bulb containing sulphuric acid, then with a weighed potash bulb followed by a weighed soda-lime tube which was guarded from the air by an unweighed soda-lime tube. The third hole in the stopper of the Erlenmeyer contained a separatory funnel containing about twice the quantity of recently boiled 10 per cent. hydrochloric acid theoretically required to liberate all of the  $\text{CO}_2$  from the sample of calcite.

The assay was made as follows: Air was drawn for about 15 minutes through the apparatus by means of an aspirator attached to the soda-lime guard tube, thus the air entered the train of potash bulbs and was depleted of  $\text{CO}_2$ , it then entered the Erlenmeyer containing the sample and then in turn the calcium chloride tube and sulphuric acid bulb which depleted it of moisture. The air then entered the weighed potash bulb from which it took up some moisture and which it then deposited in the weighed soda-lime tube which was guarded against the moisture and the  $\text{CO}_2$  of the air and aspirator, by the unweighed soda-lime tube at the end of the train. The weights of the weighed potash bulb and soda-lime were then obtained and any variation from their previous weights was noted. The weighed potash bulb and soda-lime tube were replaced in the train, the current of the air was re-established and the 10 per cent. hydrochloric acid in the separatory funnel was allowed to drip into the Erlenmeyer where it came into contact with the calcite and liberated  $\text{CO}_2$  which was dried by passing through the calcium chloride tube and sulphuric acid bulb and then caught by the weighed potash bulb and soda-lime tube. The air was allowed to pass for 15 minutes, during which time the contents of the Erlenmeyer were stirred up by the current of air and warmed a trifle by external heat. The weighed potash bulb and soda-lime tube were then allowed to stand in the balance case for about 15 minutes and weighed. When not connected in the train, the ends of the weighed potash bulb and soda-lime tube were kept closed by small rubber nipples which were removed momentarily and then replaced before each weighing in order to insure absence of pressure or vacuum within the bulb and tube. The increase in weight of the potash bulb and tube corrected as found necessary by the blank was considered to be due to the  $\text{CO}_2$  from the calcite and was calculated into terms of  $\text{CaCO}_3$ .

Results..... No. 1— 99.57

2—100.50 Av., 100.03 per cent.  $\text{CaCO}_3$

No. 4. Precipitating as calcium oxalate and weighing as calcium oxide.

In all respects this method was similar to No. 1 with the exception that the calcium oxalate after gentle ignition was made into a paste with water and spread around the sides of the crucible so that the calcium oxide would be obtained in a very thin layer. This was found essential because of the tenacity with which calcium carbonate retains its carbon dioxide. Finally the crucible and its contents

were ignited to constant weight before a blast lamp and the weight was corrected for the filter ash.

Results..... No. 1—99.75  
2—99.98      Av., 99.86 per cent.

No. 5. Precipitating as calcium sulphate and weighing as such.

0.5 Gm. of the calcite was freed from silica and iron and aluminum oxides as mentioned under "Methods of Determining Impurities." The filtrate from the iron and aluminum oxides was treated with a slight excess of dilute sulphuric acid and the solution was diluted with twice its volume of alcohol. The precipitate of calcium sulphate was allowed to settle over night, filtered off, washed thoroughly with alcohol, dried and ignited separately from the filter using only a cherry-red heat for ignition. The weight of ignited  $\text{CaSO}_4$  was then corrected for filter ash and calculated to  $\text{CaCO}_3$ .

Results..... No. 1—99.64  
2—99.73      Av., 99.68 per cent.

No. 6. Precipitating as calcium oxalate and weighing as calcium sulphate.

A 0.5 Gm. sample of the calcite was treated as in Method No. 1 to obtain the calcium oxalate which was then separated from the filter. The filter was ignited and the calcium oxalate was then placed in the crucible. A little 10 per cent. sulphuric acid was then added to the contents of the crucible which was then thoroughly dried on a water bath and very carefully ignited with the cover on, gradually increasing the heat until a cherry-red heat was attained. The crucible and contents were then weighed. The treatment with sulphuric acid was repeated until constant weight was obtained upon subsequent weighings.

Results..... No. 1—100.15  
2—100.64      Av., 100.39 per cent.

No. 7. Precipitating as calcium oxalate and titrating with potassium permanganate.

The sample of calcite was treated as in Method No. 1 to obtain the calcium oxalate which was filtered off, washed with hot water until free from soluble oxalate, transferred to the beaker in which it was precipitated by spreading the filter paper against the side of the beaker and washing down the precipitate first with hot water and then with dilute sulphuric acid (25 per cent.); reserving the washed filter by hanging it across the edge of the beaker; 50 Cc. of water

was then added followed by 10 Cc. of concentrated sulphuric acid; the solution was heated just to boiling and then titrated to the first pink change with 0.1 *N* potassium permanganate; then the filter paper was dropped in causing the pink color to be discharged owing to the trace of oxalate still present in the paper and finally the end point was obtained by a few drops of the 0.1 *N* potassium permanganate. The permanganate was standardized against calcium carbonate obtained from the standard calcite as in Method No. 2. This calcium carbonate was considered as being 100 per cent.  $\text{CaCO}_3$ . The method of standardization was as follows:

A weighed portion of the freshly ignited  $\text{CaCO}_3$  (free from  $\text{CaO}$ ) was dissolved in hydrochloric acid and precipitated as calcium oxalate as mentioned under "Methods of Determining Impurities," and this calcium oxalate was dissolved in sulphuric acid (25 per cent.) and hot water as mentioned a few lines above and the permanganate solution run in to the end point, including the few additional drops required by adding the washed filter upon which the oxalate was collected, to the titrated liquid.

Results.....	No. 1—99.91	
	2—99.46	
	3—99.90	
	4—99.47	Av., 99.68 per cent.

No. 8. Precipitated as calcium oxalate from a slightly acid solution.

A 0.5 Gm. sample of the calcite was dissolved directly in dilute hydrochloric acid; the solution was diluted to 150 Cc. and made barely alkaline with freshly distilled ammonia; a hazy precipitate of ferric and aluminum hydroxides resulted; hydrochloric acid was added drop by drop until acid, then 2 drops in excess was added. The mixture was then boiled and the calcium totally precipitated as calcium oxalate by means of an excess of ammonium oxalate solution. The precipitated calcium oxalate was allowed to settle and was then filtered off and titrated with 0.1 *N* potassium permanganate as in Method No. 7.

Result..... 99.82 per cent.  $\text{CaCO}_3$

The experiment was repeated using acetic acid to dissolve the calcite and adding 2 drops of acetic acid in excess before precipitating with ammonium oxalate.

Result..... 99.91 per cent.  $\text{CaCO}_3$

Discussion of Method No. 8. The results obtained by this method indicate that calcium can be precipitated quantitatively as oxalate from a slightly acid solution. The acidity of the solution is due solely to the presence of oxalic acid which is liberated by the slight excess of hydrochloric acid or acetic acid present in the solution. This fact is made use of by Meade for the rapid determination of calcium in cement without previous separation of silica and ferric and aluminum oxides. The method described by Meade is essentially as described above with the following exceptions: The acid solution of the cement is rendered just alkaline with ammonia and then 10 Cc. of a 10 per cent. solution of oxalic acid is added to render the mixture acid and redissolve the hydroxides of iron and aluminium which are partially precipitated when the mixture is rendered alkaline with ammonia. In order to test the value of Meade's method a sample of limestone yielding the following analysis by Method No. 7 was employed as a standard:

SiO <sub>2</sub> .....	3.320	
	3.300 Av.,	3.310 per cent.
Fe <sub>2</sub> O <sub>3</sub> -Al <sub>2</sub> O <sub>3</sub> .....	1.030 Dup.,	1.030 per cent.
CaCO <sub>3</sub> .....	77.130	
	77.125 Av.,	77.127 per cent.
MgCO <sub>3</sub> .....	18.377	
	18.332 Av.,	18.355 per cent.
<hr/>		
Total., 99.822 per cent.		

Meade's method was applied in detail to a sample of this limestone with the one exception that the calcium oxalate was finally weighed as calcium sulphate according to Method No. 6, instead of being titrated by permanganate as required in Meade's Method. The yield of CaCO<sub>3</sub> was 77.18 per cent. Another assay was made using acetic acid to dissolve the limestone and a yield of 77.31 per cent. CaCO<sub>3</sub> was obtained.

No. 9. Liberation of CO<sub>2</sub> by dilute hydrochloric acid and calculating loss of CO<sub>2</sub> into terms of CaCO<sub>3</sub>.

The apparatus known as "Geissler's new form carbonic acid determination apparatus," listed on page 103 of the catalogue of Eimer and Amend, New York, was employed.

The method consists of treating a weighed sample of the calcite in the apparatus with dilute hydrochloric acid and drawing the liberated CO<sub>2</sub> through the sulphuric acid compartment of the appa-

ratus; the entrance and exit of the apparatus being properly guarded by bulbs containing concentrated sulphuric acid.

Results..... 99.68  
99.93 Av., 99.80 per cent.  $\text{CaCO}_3$

#### No. 10. Residual titration method.

A 0.5 Gm. sample of the calcite was placed in a flask connected with a straight tube reflux condenser. A measured excess of 0.2  $N$   $\text{H}_2\text{SO}_4$  was run into the flask. The flask was connected with the reflux condenser and heated by a flame until the reaction was complete. The condenser was then washed with water, allowing the washings to flow down into the flask and the excess of 0.2  $N$   $\text{H}_2\text{SO}_4$  was titrated with 0.1  $N$   $\text{Na}_2\text{CO}_3$ , using methyl orange as indicator. The 0.1  $N$   $\text{Na}_2\text{CO}_3$  was standardized by accurately weighing out the proper quantity of freshly ignited, chemically pure sodium carbonate and the 0.2  $N$   $\text{H}_2\text{SO}_4$  was standardized against the 0.1  $N$   $\text{Na}_2\text{CO}_3$ .

Results..... 99.66  
99.83 Av., 99.75 per cent  $\text{CaCO}_3$

For convenient comparison the results are herewith presented in tabular form:

Theoretical  $\text{CaCO}_3$  content of standard material, 99.959 per cent.

Method.		$\text{CaCO}_3$ Found.
No. 1 —Precipitating as calcium oxalate and weighing as calcium carbonate...	99.64 99.49	Av., 99.57 per cent.
No. 2—Precipitating as calcium carbonate and weighing as such.....	100.05 100.10	Av., 100.07 per cent.
No. 3—Liberating $\text{CO}_2$ with $\text{HCl}$ and weighing liberated $\text{CO}_2$ in $\text{KOH}$ solution	99.57 100.50	Av., 100.03 per cent.
No. 4—Precipitating as calcium oxalate and weighing as calcium oxide.....	99.75 99.98	Av., 99.86 per cent.
No. 5—Precipitating as calcium sulphate and weighing as such.....	99.64 99.73	Av., 99.68 per cent.
No. 6—Precipitating as calcium oxalate and weighing as calcium sulphate....	100.15 100.64	Av., 100.39 per cent.

Method.	CaCO <sub>3</sub> Found.	
No. 7—Precipitating as calcium oxalate and titrating with potassium permanganate.....	99.91 99.90 99.46 99.47 Av.,	99.68 per cent.
No. 8—Precipitating as calcium oxalate from a slightly acid solution.....	99.82 99.91	Av., 99.87 per cent.
No. 9—Liberation of CO <sub>2</sub> by HCl and calculating loss of CO <sub>2</sub> into terms of CaCO <sub>3</sub> .....	99.68 99.93	Av., 99.80 per cent.
No. 10—Residual titration method.....	99.66 99.83	Av., 99.75 per cent.

PHARMACEUTICAL LABORATORIES,  
H. K. MULFORD CO.,  
PHILA., PA.

## PHILADELPHIA COLLEGE OF PHARMACY.

### SPECIAL MEETING.

A special meeting of the Philadelphia College of Pharmacy was held April 26, at 3 P.M., to hear the reports of the Organization Committee on Centennial Celebration.

The Executive Secretary of the Committee, Professor E. Fullerton Cook, read the report.

At the Annual Meeting of the College, held March 29, 1920, following the discussion of the Centennial Celebration of the founding of the College, the President was directed to appoint a committee to prepare plans for a suitable celebration. The President appointed on this committee Dr. R. V. Mattison, Aubrey H. Weightman, representing the college; George M. Beringer, Wm. L. Cliffe, Joseph W. England, for the Board of Trustees; Charles H. LaWall, E. Fullerton Cook and F. P. Stroup, for the Faculty, and Otto Kraus, R. P. Fischelis, for the alumni. The Board approved the appointments, as also that of E. Fullerton Cook as Executive Secretary.

The Organization Committee has held a number of meetings and make the following recommendations:

First, *Time*.—It is suggested that the entire Commencement Week in June, 1921, be utilized for the main Centennial Celebration.

Second, *Funds*.—It is essential for the proper carrying out of the



programme, and the establishment of the College on a plane which is worthy of its past, and which will establish a proper endowment for its future development, be established. It is believed that it will be necessary to secure *Two Million Dollars*. This should be our avowed aim for an ample endowment and building fund for the Philadelphia College of Pharmacy.

In the campaign for funds three separate classifications are suggested:

- |                                 |                         |
|---------------------------------|-------------------------|
| A.—Endowment                    | { Fellowships           |
|                                 | { Professional Research |
|                                 | { Library               |
| B.—Buildings                    |                         |
| C.—Maintenance and Development. |                         |

That donors may assign their contributions to any of these three purposes, and it is hoped that suitable memorial buildings, professorships and laboratories may be established.

Third, *Coöperation from Other Associations*.—Pharmaceutical Associations be invited to arrange to hold their annual meetings in 1921, in Philadelphia, or if this be impossible, to send delegates to the College Centenary Celebration. A letter of invitation has been prepared and will be sent to the various associations. The Committee desires to suggest that the Centennial Celebration of the Philadelphia College of Pharmacy be made broad and useful to the profession by emphasizing the fact that it is the Centennial of the establishment of pharmaceutical education in America.

Fourth, *Centennial Volume*.—The sub-committee on Centennial Volume, Mr. George M. Beringer, chairman, presents the following tentative report: It is difficult at this time to present a complete outline of what the Historical Volume should contain; so this report must be viewed as only a tentative suggestion for the contents of the proposed volume.

1. History of the College.—This will lead to chapters on the influence of the College upon pharmaceutical education, Pharmacopoeial and National Formulary revisions, State and National Organizations, Industrial and Trade Developments, Medical Practices, Legislation, etc. Included in this will be the History of the Department of Pharmacy of the Medico-Chirurgical College.

2. History of the Combined Alumni.—This should be a distinctive feature, and in connection therewith short biographies of

each graduate should be given, if available. These can possibly be best presented with the sketch of each graduating class, and in addition an alphabetical list of all the graduates should be included.

3. History of each member of the Faculty since the Foundation of the College.—This can well be made a leading part as most of these have been men of ability and marked influence upon the events of their day, and moreover the Alumni have a warm sentiment for their old professors.

4. History of the Officers and Prominent Members of the College.—Our history is replete with the efforts and services of many eminent men whose work in behalf of pharmacy, the college, and public welfare, should be permanently recorded in such a volume.

5. History of the AMERICAN JOURNAL OF PHARMACY and its Editorial Management, during more than Ninety Years of its Publication.

6. The Story of the Library, Museum and Herbarium and of the Laboratories.

7. The Centenary.—Full account of the celebration, plans and functions. As the plans develop, doubtless many other subjects that must be included in the Centennial Volume will become evident.

If it is determined to issue a volume such as is outlined herewith, the enormity of the task must be appreciated, and an active committee should be appointed at an early date. The preparation of the manuscript will entail much time, labor and expense. The committee should have authority to employ such outside assistance as may be necessary.

We cannot at this time gauge the possible expense of this project. Your committee are of the opinion that the College should be largely reimbursed for this expense by the sale of the volume.

Fifth, *General Committee on Centennial*.—This large General Committee, not limited to one hundred, as first proposed, shall consist of members of the College, alumni and friends of the College. It shall represent all activities into which our alumni have entered and all geographical sections where they may reside. The following classification has been suggested:

Officers of the College.

Members of the Board of Trustees.

Faculty of the College.

Pharmacists	{	Men Pharmacists
		Women Pharmacists
		Army Pharmacists
		Navy Pharmacists

Physicians

Wholesale Druggists

Chemical Manufacturers.

Pharmaceutical Manufacturers.

Editors and Journalists.

Chemists.

Members of State Boards of Pharmacy.

Salesmen.

The President of the College shall be the chairman of this General Committee.

#### SUB-COMMITTEES.

It is further suggested that there shall be established sub-committees on

1. Site.
2. Contributions.
3. Historical Data and Centennial Volume.
4. Plans for the Centennial Celebration.
5. College Membership.
6. Publicity (including conventions).

Executive Committee.—The chairmen of these special committees, acting with the President of the College, shall constitute an Executive Committee who will be immediately responsible for the carrying out of the plan.

Campaign Funds.—The organization committee suggests that the members of the College approve an appropriation by the Board of Trustees of \$10,000, to provide funds for necessary expenses.

Site.—The President and other members have been in communication with the Mayor and other officials of the City and the Fairmount Park Commissioners concerning a suitable location upon the parkway for the new college buildings.

Buildings.—The President announced that Mr. Horace Trumbauer, one of the most prominent architects of Philadelphia, is now drawing plans for the new college buildings.

The programme thus placed before the members of the college calls for a unity of purpose, an enthusiasm and a faith in the institution and its future which will be worthy of the traditions of the Philadelphia College of Pharmacy. Always a leader, always maintaining

the highest ideals, the opportunity is offered our alumni and friends to place the college on a permanent foundation for the second hundred years of its history. Every alumnus is proud of the college. Each will be honored by its increased pre-eminence among scientific organizations, and by the status which pharmacy must assume in the development of modern medical practice. Pharmacy fixed upon the professional plane which is thus assured, will continue its great service to the medical profession and to humanity at large and will thus increase its prestige and distinction.

The report was received and the recommendations considered seriatim.

Many of the members took part in the discussion that followed the consideration of each recommendation and the report with only several slight amendments was adopted as a whole.

Dr. Robinson asked consideration of the plan proposed at the annual meeting of enlisting the coöperation of those graduates of the College who are now practicing medicine. He thought there were about 250 of these graduates in Philadelphia or vicinity alone. He suggested an organization be formed to be called "The Medical Section of the Alumni of Philadelphia College of Pharmacy. The title was approved and it was believed this section would be a valuable help in the Centennial efforts.

There was some discussion as to the continuance of the General Committee on Centennial, when, on motion, it was voted that the committee be continued as an Advisory Committee.

C. A. WEIDEMANN, M.D.,

*Recording Secretary.*

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## ISOLATION OF THE ACTIVE PRINCIPLE OF THE THYROID GLAND.\*

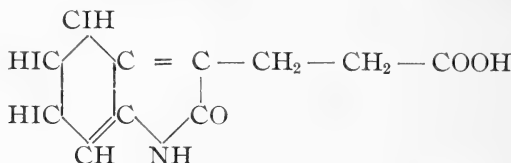
Among the achievements of biological chemistry the isolation in a crystalline form, and as a definite chemical body of the blood-raising principle present in the suprarenal capsule marks a distinct epoch, and the investigations to which adrenalin has since its discovery been submitted have removed the veil from many processes connected with the life of the organism. Now comes the news from America of another great stride forward in our knowledge of biology, of a discovery that may have far-reaching effects on thera-

\* From *The Chemist and Druggist*, March 27, 1920.

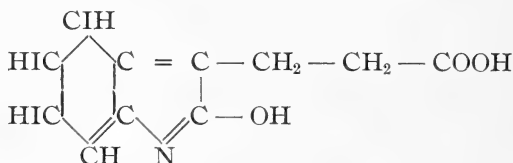
peutics. E. C. Kendall, working in the clinic of the Brothers Mayo, of Rochester, has succeeded in isolating in a crystalline form the iodised active principle of the thyroid gland, that mysterious body which seems to play such an exceedingly important rôle in living processes. In the *Journal of Biological Chemistry* (Vol. xxxix.) he reviews his investigations on this point, which began as far back as 1910. At first he used barium salts to separate this substance, to which the name of "thyroxin" has been given, and first succeeded in isolating it in December, 1914, the total amount obtained being 100 milligrams. In February, 1916, the action of carbonic acid on the process of isolating this body was discovered, resulting in the production of 7 grams by May, 1917. This amount was used to ascertain the chemical structure of the new body, and based on these findings. Osterberg succeeded in preparing a small quantity of thyroxin by synthetic methods. At the time of publishing his paper, the author had succeeded in preparing about 35 grams of thyroxin from 3,275 kilograms of fresh thyroid glands, obtained almost exclusively from pigs. The yield consequently works out at the ratio of 1 gram of thyroxin for 100 kilograms of thyroid gland. The following process was adopted: The fresh thyroid glands are hydrolysed in a 5 per cent. soda solution. The fats are removed by being transformed into insoluble sodium soap. The alkaline filtrate is acidified after cooling, and the precipitate thrown down contains practically the whole of the thyroxin present. This precipitate is separated and dissolved in a solution of soda, and again precipitated by the addition of hydrochloric acid. The precipitate, after drying at ordinary temperatures, is dissolved in alcohol (95 per cent.), and to neutralize the remaining excess of hydrochloric acid present in this dried precipitate, solution of soda is added, which gives rise to a compact, black and sticky precipitate, which is separated by filtration. To the alcoholic filtrate a very concentrated, hot aqueous solution of barium hydroxide is added, and the mixture is boiled under a reflux condenser to remove all the impurities and coloring matter present. A trace of soda is added to the filtrate, through which a current of carbonic acid gas is passed, whereupon the carbonates which have formed are removed by filtration, and the alcohol by distillation. Hydrochloric acid is now added to the aqueous solution, the precipitate thrown down is dissolved in an alkaline alcoholic solution, and the latter saturated with carbonic acid gas. The solution is filtered, the alcohol removed by dis-

tillation, and after standing for a time the mono-sodium salt of thyroxin separates out. The latter is purified by dissolving it in an alkaline alcoholic solution, then saturating with carbonic acid gas and distilling off the alcohol; the same operation may be repeated five or six times, using acetic acid in the place of carbonic acid, until the thyroxin as "4-5-6-hydro-4-5-6-iodo-2-oxy- $\beta$ -indolpropionic acid," of the empiric formula  $C_{11}H_{10}NO_3I_3$ .

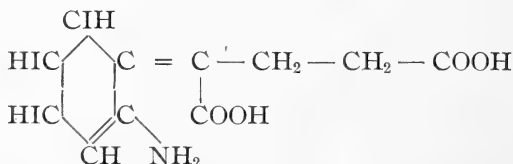
It occurs in three different forms: (1) A ketonic form:



(2) A tautomeric enolic form:



(3) With an open pyrrolic nucleus, due to fixation of  $H_2O$ , so that this body possesses both the characters of a di-acid and of a primary amine:



The author states that the first form is the anhydride of the third, and these bear the same relationship to each other as creatinin to creatin. The third form is, therefore, "thyroxin," and occurs as such in the thyroid gland; it cannot be obtained in crystalline form, but crystallizes only on being converted into its anhydride. Kendall found that during the months of January, February and March the glands contain only a slight percentage of thyroxin, whereas during the summer months there is an increase amounting to 400 per cent., and this is the time when the glands should be used for the extraction of their thyroxin.

## DEVELOPMENT OF KAURI GUM INDUSTRY IN NEW ZEALAND.\*

BY CONSUL GENERAL ALFRED A. WINSLOW,  
AUCKLAND, FEBRUARY 10, 1920.

Since the close of war more attention has been given to the development of the kauri-gum industry in New Zealand than any time during the past five years, with the result that it seems probable that greater quantities of kauri gum and its by-products will be produced than heretofore.

*Oil from Kauri Peat Swamps.*—There are very extensive kauri peat swamps in New Zealand that have been placed at the disposal of interested parties by the New Zealand Government on a leased basis. The present area for which the Governor General by Order in Council may set apart for the development of this industry is 10,000 acres on a basis of leases for 42 years, with no party to receive a lease exceeding 3,000 acres. The lessees have to pay a low rental and also a royalty on kauri oil and other valuable products obtained.

The New Zealand Peat Oils (Ltd.) have taken one grant of 3,000 acres, and are now developing it with reasonably good prospects of success, having tested four samples taken from different depths of the swamp which yielded an average of 29 gallons of crude kauri-gum oil to the ton, with a yield of 4,300 cubic feet of gas per ton. This company proposes to push the development of this industry during the coming year.

*Kauri Gum Extraction and Grading.*—A new method of gathering and grading kauri gum has lately been undertaken, whereby kauri peat swamps that are thoroughly pregnated with kauri gum in different stages of decomposition can be worked with reasonably good success, according to late reports. It is claimed that if this process succeeds, as indicated at present, there can be more kauri gum secured from the deposits in the North Island than has been secured to date, though of an inferior grade to that which has been gathered.

It is proposed to grade this kauri gum into about three or four grades according to size, which means largely according to the degree of composition. It is claimed any grade would be sufficient in quality for the manufacture of the lower grades of varnishes and similar products, and would be exceptionally good for the manufacture of linoleums and that line of goods; and it is expected that

\* From *Commerce Reports*, April 8, 1920.

these qualities of kauri gum can be produced in such quantities as to be sold for a very much more reasonable price in proportion to what kauri gum has been sold for heretofore.

*Production of Kauri Gum.*—The production of kauri gum during the seven years previous to the beginning of the war averaged not far from 8,000 tons per year, while since that time it has scarcely averaged 4,000 tons, and during the year ended, March 31, 1919, only amounted to 2,338 tons. Of the output of 8,473 tons for 1914 the United States took 4,531 tons, the United Kingdom 3,335 tons, Germany 373 tons, and the remainder was well scattered over 10 other countries; while for the year ended March 31, 1919, the United States took 1,371 tons of the 2,338 tons, while the United Kingdom took 346 tons, Canada 572 tons, and Australia 49 tons.

Of late quite large quantities of kauri gum have been going forward to the United States as shipping space could be obtained, and there are still large quantities in hand here for export, and it would seem there would be no difficulty in getting all of the kauri gum necessary from now on.

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#### ELEMI.\*

Elemi is a drug very little used in modern pharmacy, being chiefly employed in the form of a stimulating ointment in naval surgery, and finding a place for that purpose in the medicine-chests kept on board ships, foreign as well as English. It has, however, a much wider employment in the manufacture of printing-ink, in which its viscosity and adhesiveness and honey-like consistence are of considerable advantage. It is of use also in felting and varnish making and plasters. In the *Scientific American* attention is directed to the elemi of Porto Rico, derived from *Dacryodes hexandra* Griseb., and known in that island under the name of Tabanuco. This tree is the best timber-tree of the island, the trunk attaining a height of 50 feet to the first branch, and a diameter of 5 feet near the base. When the smooth bark is tapped by V-like incisions formed by two oblique strokes of the hatchet, the oleoresinous juice flows out and is collected in vessels when it is to be used for medicinal purposes, being employed in native practice as a stimulant ointment for indolent ulcers. It is also used for torches and as incense. For torches the juice is allowed to run down a central stick and formed

\*From *The Chemist and Druggist*, March 20, 1920.



into a cylinder and covered with the leaf of the royal palm. As the volatile oil evaporates a solid candle or torch is formed. For incense also the oleoresin is allowed to solidify. But the tree is not confined to Porto Rico, as it occurs in several of the lesser Antilles Islands and in Costa Rica, where it is also known by the same name, Tabanuco.

In Dominica it is known as the *Gommier* or *Gommier rouge*, and is believed to be the source of the elemi of that island. In St. Lucia it is called the *Gommier à Canot*. But the word *Gommier* may almost be taken as synonymous with elemi, since the various trees called by that name yield an oleoresin having most of the properties of elemi, though differing somewhat in odor from the Manila elemi of the Philippines, which was formerly official in various Pharmacopoeias. Thus the *Gommier* of the Windward Islands is *Bursera gummifera* Linn., known in Jamaica as the birch-tree, and in St. Vincent as the turpentine tree. A second *Gommier* in St. Lucia is the *Protium Guianense* March, which is distinguished as the *Gommier à l'encens*. It yields also the *encens* of Cayenne and the *Tacamahaca* of Venezuela. All these trees belong to the same natural order *Burseraceae*, to which also the frankincense tree of Somaliland belongs. There has been much confusion regarding the botanical names of the trees yielding the different kind of elemi, or oleoresins that have been imported into Europe from time to time under these names. Thus Manila elemi was for many years attributed to *Canarium commune*, and it is only since the American occupation of the Philippine Islands that it has been shown to be the product of *Canarium Luzonicum* Miq., and partly of *Canarium villosum*, Benth. and Hook. f. It may be regarded as probable, however, that African elemi from Angola is yielded by *Canarium edule*, Hook f., and that of Central Africa, Uganda and Southern Nigeria by *Canarium Schweinfurthii*, Engl.; Mexican elemi by *Amyris Plumieri*; British Guiana by *Protium Guianense*, March, and *P. heptaphyllum*, March; Brazilian elemi by *Protium Icicariba*, March; and Mauritius elemi by *Canarium Mauritianum*, Blum. It is therefore evident that various oleoresins more or less resembling Manila elemi occur in tropical countries in various parts of the globe, and are possibly capable of commercial use. At present few of them, except the Manila elemi and the *Gommier à l'encens* of the West Indies, are collected in a clean condition, and most of them are not even purified by melting and straining.

The essential oils of these oleoresins have in a few cases been examined and some of their constituents determined. Thus in Manila elemi and that of Southern Nigeria and of Uganda the odor of phellandrene is prominent. Limonene is also present in some varieties, and in one terpinene and terpinolene. But the possible uses of these oils in varnish making and in perfuming soap have yet to be worked out.

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### EFFECTS OF QUININE ON THE TISSUES.\*

There are circumstances in which the vigorous action of adequate quantities of quinine in the circulation is highly desirable. The alkaloid itself is rather insoluble; but some of the salts of quinine are fairly soluble, and are absorbed with considerable readiness from the gastro-intestinal canal. The "Pharmacology of Useful Drugs,"<sup>1</sup> issued by the American Medical Association, makes it seem probable that too much importance has been attached to the influence of the degree of solubility of the salts of quinine in their absorption, and too little attention to the selective capacity of the gastro-intestinal tract for absorbing them. In the United States, in contrast with European countries, quinine sulphate is the salt generally prescribed, although the hydrochloride is decidedly more soluble and ought to be preferred. However that may be, numerous endeavors have been made to secure more effective quinine therapy, particularly in malaria, by modes of administration other than the usual oral path.

Baccelli first suggested the intravenous injection of solutions of salts of quinine when the symptoms of malaria are so severe as to threaten grave peril to the patient. Subcutaneous or intramuscular injection has also been recommended and frequently employed, particularly in critical cases. Despite the use of care in giving such treatment, much discomfort and pain may be caused; and even if aseptic precautions are studiously applied, a considerable amount of induration if not actual abscess formation is likely to occur at the site of injection. Most therapeutists recognize this danger and warn against it.

That tissue necrosis is produced by strong solutions of quinine salts need not be a surprise when it is recalled that for more than

\* From *Jour. Amer. Med. Assoc.*, Feb. 14, 1920.

<sup>1</sup> Hatcher, R. A., and Wilbert, M. I.: "Pharmacology of Useful Drugs," Chicago, *Amer. Med. Assoc.*, 1915.

half a century the substance has been regarded by toxicologists as a protoplasmic poison capable of destroying various forms of animal and vegetable cells. The suggestion has at times been made that, because of the observed tissue damage following intramuscular injections, this mode of administration should be abandoned. A recent experimental inquiry by Colonel Dudgeon<sup>1</sup> of the British Army Medical Service, on the effects of injections of quinine into the tissues throws new light on the actual conditions developed by the procedure. It has been suggested that in order to avoid the untoward results, intramuscular medication should be carried out only with dilute solutions. Dudgeon points out, however, that injection of quinine in solutions so dilute as to avoid edema and tissue necrosis is not of practical utility in man. Concentrated preparations of quinine produce more intense necrosis than do dilute ones; but when the latter are such as to be of therapeutic value, they also excite the tissue changes at the site of infection.

A concentrated solution of quinine is absorbed rapidly from the tissues even in patients who are moribund. Dudgeon insists on the necessity of realizing that tissue necrosis—spreading edema and local blood destruction—are produced by the solvents frequently employed for quinine administration; and the effects are only slightly inferior to those excited by the quinine salts and the alkaloid. No advantage was gained by the addition of oil or by injecting the alkaloid dissolved in alcohol or ether. Necrosis of blood vessels in the area of injection is a common result. This leads, according to Dudgeon, to hemorrhages into the tissues. Extensive damage of these sorts in the neighborhood of an important nerve trunk may result in nerve palsy.

It may be that a choice between disadvantages will dictate the continuance of intramuscular injections of quinine. If so, the limitations and dangers of their use in practice need to be appreciated clearly and specifically. Daily doses administered for periods of a week and more in the gluteal region—a favorite site for injection—are not unknown. Such cases have been found, further, to retain only fragments of healthy tissues in the muscular tracts involved. Hence one can appreciate the force of Dudgeon's warning that repeated intramuscular injections of quinine should not be given into the same area of muscle or tissue directly adjacent, because otherwise permanent injury of muscle or nerves may result.

<sup>1</sup> Dudgeon, L. S.: "On the Effects of Injections of Quinine into the Tissues of Man and Animals," *J. Hyg.*, 18: 137 (Oct.), 1919.

THE CULTIVATION OF MEDICINAL PLANTS IN FRANCE  
AND THE FRENCH COLONIES.\*

A very interesting account has recently been published<sup>1</sup> of the development of the movement instituted in Paris in the early years of the war for extending the cultivation in France and French Colonies of medicinal plants and plants used for the production of volatile oils. The following brief review of the progress made and of the organization adopted shows the energy displayed by the French in their endeavor to rehabilitate what was formerly a prosperous industry and to free themselves from dependence upon foreign countries for raw material. The support which the movement has received from the Government through the Ministry of Commerce and Industry stands in sharp contrast with the treatment received by a similar movement in this country.

France has gradually lost by foreign competition the premier position which it formerly occupied in the collection and cultivation of medicinal plants, and has consequently been compelled to purchase these, chiefly from Germany and Austria, to the value of nearly 20 million francs yearly. When these supplies were cut off by the war she had perforce to foster both collection and cultivation.

The first attempts, praiseworthy as they were, failed to produce results of immediate value, and it was found necessary to coördinate isolated efforts. The importance of the work has already been publicly recognized. The Minister of Commerce and Industry urged on the President of the Republic the desirability of appointing a committee to organize and increase the cultivation, collection and preparation of medicinal plants, and in 1918 a Committee of Medicinal Plants was officially formed. The President of this Committee was a professor of the Museum of Natural History and the Vice-Presidents were a professor of the Faculty of Science and a professor of the Ecole Supérieure de Pharmacie. Among the twenty-six members of the Committee were representatives of the Colonial Office, of the Jardin Colonial, of the Ministry of Agriculture, of the Ministry of Public Instruction, of the Ministry of Commerce, of the Association Générale des Herboristes de France, of the Association des Syndicats Pharmaceutiques de France, etc. An exceedingly strong

\*From *The Pharm. Jour. and Pharmacist*, March 6, 1920.

<sup>1</sup> "Le Comité interministériel des Plantes Médicinales et des Plante à Essences: Son Histoire, ses Buts, ses Moyens d'Action." Lucien Declume, 1919.

committee, standing in direct communication with the State, with the Universities and with various industrial companies and syndicates, was thus constituted, and it immediately set to work. Commissions for economic studies and propaganda, for cultivation and collection and for the cultivation of exotic plants were formed.

The Commission for Economic Studies and Propaganda decided to form regional committees in order to procure without delay local information and to arrange between collectors and consumers the price at which the drugs should be sold.

The Commission for Collection and Cultivation busied itself with instructions to collectors, with the provision of samples, with pamphlets, and so on. The value of special drying sheds was recognized, but as rapidity was essential it was decided to employ the simple methods already in use. The representative of the Ministry of Public Instruction undertook to include in the official publications any notes or articles which the Committee might compile, and indicated his intention of sending to the provincial schools illustrated descriptive leaflets of common medicinal plants, together with the mode of collection, etc. The journals of the pharmaceutical and agricultural syndicates were also utilized for this purpose, and one number of *La Française* was almost entirely devoted to the subject. The necessity of furnishing all indispensable details before recommending the cultivation of any particular plant was recognized as was also the danger of extermination by indiscriminate collection.

The Commission for the Cultivation of Exotic Plants had to deal with a most extensive programme, as France has to procure the majority of the overseas drugs she uses from foreign countries. The Committee of Medicinal Plants put themselves in communication with the Directors of Agriculture in the French Colonies in order to obtain technical assistance. Particular attention was directed to the cultivation of senna in Morocco, Guinea, Dahomey and Madagascar; of the poppy in Morocco; of *santonica*; of *buchu* in Northern Africa; of *Strophanthus hispidus* and *S. Kombé* in Gaboon and Dahomey; and of cocoa in Dahomey. Soils of proposed sites for cultivation were to be analyzed, and the endeavor made to secure special facilities for artificial manures. The Commission also dealt with the important subject of *cinchona*. The mountains of Annam were recommended as offering favorable conditions of soil and climate, and the Governor-General of Annam was approached on the subject, the merchants present placing 6000 francs a year at the

disposal of the Commission to facilitate the carrying out of experiments. M. Alland, the premier gum importer of France, was requested by the President (Professor Perrot) to give an account of the cultivation of the gum acacia tree, the result of which was that the Commission decided to communicate with the Governor-General of Senegal with the view of developing in that colony the cultivation of gum-bearing acacias.

Soon after these decisions had been arrived at, the Committee of Medicinal Plants began to consider ways and means. A substantial income was necessary if the work of the Committee was to bear fruit. It was resolved that the endeavor should be made to obtain an annual grant of 50,000 francs from the State, and an additional 150,000 francs from those industrially interested in the work. Such an income would allow of financial assistance being given to defray the expenses of experimental trials, of technical researches in University laboratories, of investigating cultivation in the tropics, of the maintenance of an office, and so on. A grant of 50,000 francs for a year (renewable, it is hoped), was readily obtained from the State.<sup>1</sup>

In the meantime the Inter-Ministerial Committee had organized no fewer than fifteen Regional Committees in France, one in Algiers, and one in Tunis; in each case the Regional Committee consisted chiefly of professors of the local university or school of medicine and pharmacy or similar institutions, together with pharmacists, druggists, herb-growers, etc. As the result of inquiries, the approximate quantities required of the most important indigenous drugs had been determined, and, in conjunction with the Syndicate of Druggists, a basis of prices had been arranged.

It was now considered desirable to establish an "Office National des Matières premières pour la Droguerie, le Pharmacie, la Distillerie et la Parfumerie," and such an office was founded under the auspices of the Inter-Ministerial Committee and of the syndicates of the several industries mentioned. The object of this office is to form a Society of Study, Research and Propaganda, with the view of organizing in France a drug market and of producing drugs, so as to render the country independent of foreign markets. It is intended:

(a) To collect all information concerning the origin, cultivation and improvement of all plants and their products.

<sup>1</sup> It is understood that the additional 150,000 francs have now been subscribed, making an annual income of 200,000 francs.

(b) To centralize the technical, scientific and commercial information necessary for developing the commerce and chemical treatment of drugs.

(c) To encourage and organize in France and the French colonies the cultivation and production of raw material.

(d) To study all questions relating to the development and protection of the drug market.

(e) To give financial assistance to laboratories for all studies concerning the composition of raw material and the extraction of their active constituents—to publish the results, so that they may be utilized industrially or therapeutically.

(f) To organize and financially assist research expeditions with the view of investigating the sources of production, and of securing the seeds, rhizomes, etc., necessary for attempting their cultivation in France.

(g) To keep in communication, by means of the Ministry of Commerce, with the Agricultural Services, Technical Institutes, Ambassadors, Consulates and Commercial Agents abroad; to suggest to public authorities the initiatives to take and all actions for the extension of the production or for the exportation of raw or manufactured products.

That this admirable and extensive organization has been carried through in so short a space of time and so successfully has been largely due to the energy and foresight of Professor Perrot, of the Ecole Supérieure de Pharmacie. That it has already borne fruit is shown by the fact that Professor Perrot and M. Alland (representing, respectively, Science and Commerce), are at this moment engaged in investigating at Khartoum the cultivation of gum-bearing acacias, of senna and of other drugs, with the view of establishing them in the French colonies of Africa.

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#### TUBERCULOSIS IN 1920.\*

Lereboullet and Petit say that the prophylaxis and hygiene rather than the medical aspect of tuberculosis engrossed attention during 1919. Among the few communications on the medical features were those of the detection of the falsely labeled tuberculous.

\* From *Paris Médical*, 9: 52 (Dec. 27), 1919; through *Jour. Amer. Med. Assoc.*, Feb. 28, 1920.

Compulsory declaration of tuberculosis seems to have been postponed to the day when the declaration will ensure care and assistance for the tuberculous and his family. Until this can be realized, notification serves merely to pile up statistics. E. Sergent has recently presented evidence that even tubercle bacilli in the sputum do not necessarily prove that the lesions are in process of evolution, and also that the absence of tubercle bacilli is not unfailing testimony as to the non-activity of the lesions. Radiography throws no light on the age and evolution of the lesions, but a low arterial pressure is the rule in progressing cases. A rise in temperature after muscular exercise does not necessarily mean tuberculosis, as unstable temperature may be observed under various other conditions, digestive, cardiac, etc. They agree with Sergent's dictum that there is absolutely no certain sign which tells whether tuberculous process in a well appearing person is progressing or not. He may have had hemoptysis on one occasion or a disquieting pleurisy, but has been in apparent health since. Repeated examination, the fixity of the stethoscopic and radiosopic findings, the character of the physical signs, the attenuation of the myotonic reaction, the disappearance of the tenderness of the apex, the normal blood pressure, the intensity of the tuberculin reaction, stability of the temperature, and the repeatedly verified absence of tubercle bacilli from the sputum, form a bundle of proofs on which the diagnosis can be based. The whole secret lies in repeating the examinations and comparing the findings. About 25 per cent. of the tuberculous show Roentgen shadows in the fissures between the lobes, but few physicians ever examine for these *localisations scissurales*, and yet they are an important factor in recurring pleurisy. The stethoscope reveals small and inconstant foci of dry rattling, or friction râles, which, associated with intercostal neuralgia and cough, aid in detecting these frequent and benign tuberculous lesions.

Roger demonstrated ten years ago that the absence of albumin from the sputum excluded tuberculosis. A positive albumin reaction is found in many other diseases, but Krongold has recently published evidence to the effect that the presence of peptone in the sputum is a reliable sign of tuberculosis, as the tubercle bacilli belong to the small group of microörganisms which by their proteolytic ferments split albumin into albumoses and peptones. Jousset insists that tuberculosis, as we know it, is merely the nodular form of infection by the tubercle bacillus. The latter may induce



a wide range of reactions and symptoms, and in both there is first an acute, curable, congestive stage, in which serotherapy is promising. (His method was described in these columns, August 17, 1918, p. 235.) He draws the balance sheet with a most favorable balance to the credit of the procedure in appropriate cases. Lalesque's review of his thirty years of treatment of tuberculosis at a seashore sanatorium is said to be another instructive contribution. He emphasizes the importance of the moisture of the sea air in preventing congestion and hemoptysis.

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## A NOTE ON COBRA VENOM AND ITS EFFECTS.\*

BY HERBERT CLAYTON.

The poison excreted from the salivary glands of the cobra is regarded as one of the most deadly animal fluids known to science. When freshly excreted it is a pale yellow liquid, rather viscid, having a specific gravity of about 1.046. On exposure to air it rapidly evaporates, leaving a shining, granular residue, which has no definite crystalline form. The dried venom is readily soluble in water, and gives a feeble acid reaction. The poison has been the center of many investigations, with varied results. E. Faust claims to have shown "That the essential constituent of the cobra poison is a nitrogen free substance, belonging pharmacologically to the group of the picrotoxins, sapotoxins, and sphacelo-toxins." The victims of this reptile frequently bear very little sign of external injury, a small scratch or puncture being the only indication where the fangs have worked their havoc. The tissue lying beneath the wound is colored dark purple, and a large quantity of viscid blood-like fluid collects in the vicinity of the wound. An intense burning pain at the spot bitten is the first symptom. In man there follows an interval before fresh symptoms occur. According to Dr. Wall the average is about an hour. Once developed, the symptoms follow a rapid course. A feeling of intoxication is produced, followed by a loss of power over the limbs. The patient is bereft of speech, swallowing, and the control over the movement of the lips. The saliva is ejected in large quantities, the respiration gradually becomes slower and slower, and at length ceases.

\* From *Australian Jour. of Pharm.*, Feb. 20, 1920.

## PRODUCTION OF ATTAR OF ROSES IN BULGARIA.\*

BY CONSUL GRAHAM H. KEMPER,  
SOFIA.

During the 12 years prior to the first Balkan War, that is, from 1900 to 1912, the manufacture of attar of roses in Bulgaria attained its highest development. During that period a large number of up-to-date factories equipped with modern steam stills were erected. The total area planted to roses increased to more than 20,000 acres. Owing to the three wars in which Bulgaria has taken part since 1912, the industry of rose culture for the production of attar of roses has experienced a decided setback. It is estimated that the present acreage planted to roses is not more than 15,000.

The average annual production of attar of roses during the period from 1900 to 1912 was about 126,800 ounces. The production fell to 85,000 ounces in 1917, 85,000 ounces in 1918, and 52,000 ounces in 1919, and it is predicted that the present year's yield will show a further decrease.

During the war, owing to the fact that Bulgaria was cut off from the principal markets—New York, London and Paris—the stocks of attar of roses remaining unsold increased until they reached a total of about 275,000 ounces, about 40 per cent. of which is said to have been of inferior quality. About one-third of this total available stock was sent to the United States early in 1919 in part payment for flour imported from the United States; also some 17,000 ounces were shipped to the United States during the last quarter of the year. It is estimated that the present available stock in Bulgaria hardly exceeds 50,000 ounces, worth about \$500,000.

It is stated by one of the best-known producers that under existing conditions the production of attar of roses is not a paying industry. Owing to the high prices for other farm products, at least 5,000 acres of rose gardens have been abandoned and the land planted to more remunerative crops, especially tobacco. Centralization, by the formation of a syndicate for the purpose of eliminating unnecessary expenses, is spoken of as the only course that will save the industry.

\* From *Commerce Reports*, March 6, 1920.

## NEWS ITEMS AND PERSONAL NOTES.

**TESTIMONIAL DINNER TO PROF. COOK.**—The members of the Philadelphia Branch of the American Pharmaceutical Association and friends of Prof. E. Fullerton Cook tendered him a testimonial dinner at the City Club of Philadelphia on Friday evening, May 28th, in honor of his being elected chairman of the U. S. P. Committee of Revision. Many of the members were accompanied by their wives. The presence of Mrs. Cook and likewise the Rev. Cook and Mrs. Cook, father and mother of the guest of honor, added greatly to the sentiment and enjoyability of the occasion.

Prof. Julius W. Sturmer acted as toastmaster and introduced the speakers of the evening.

Dr. Harvey W. Wiley, of Washington, D. C., President of the Pharmacopoeial Convention for the Ninth Revision of the U. S. P., was the first speaker. He made a very happy and witty talk in which he paid a glowing tribute to the sacrificing work of the late Prof. Remington and congratulated the Pharmacopoeia upon the selection of such an able and virile new chairman for whom he predicted a very successful career in connection with the work of revision.

Prof. Charles H. LaWall and Prof. H. C. Wood as former Acting Chairmen of the Committee of Revision, expressed their appreciation of the selection of Prof. Cook as the Chairman of the Committee for the Tenth Revision and upon the successful inauguration of the work and the progress that has already been made under his leadership.

The Rev. Cook expressed his gratification that his son had developed by reason of the training of his mother into a professional gentleman with a promising and useful career and he was pleased and gratified to see the honor and the tributes which were paid to him upon this occasion.

George M. Beringer was introduced as the preceptor of Prof. Cook when he was a pharmacy student at the Philadelphia College of Pharmacy and spoke very highly of E. Fullerton Cook's personal characteristics when a student and assistant in his store. The ease with which he made and held friends and his courteous treatment of customers by which he immediately gained their confidence, were among the qualifications that were early demonstrated in his store experience, and this as well as his earnestness and perseverance

in his studies and work have been personal characteristics upon which his success had been largely built. The speaker referred to the tempestuous waves of the pre-convention period and the radical views of certain delegates that threatened danger to the voyage of "Ship Revision" and how with the election of Prof. Cook as chairman this storm was immediately calmed and a happy and successful voyage was now prophesied.

Dr. Harry Vin Arny, of New York, extended his congratulations and expressed the sentiment that the members of the Committee of Revision had arrived at the conclusion that Prof. Cook was the most logical man both as to experience and personal qualities to act as chairman of the committee and predicted that he would be continued permanently as chairman for the balance of his days.

Dr. E. G. Eberle spoke of the general approval that had followed the selection of E. Fullerton Cook as chairman, and of the conference in which the qualifications essential for the chairmanship of the Revision Committee had been discussed and in which it was concluded that Prof. Cook possessed the requisite energy, stability and ability called for.

Among the other speakers of the evening was A. Louis Seift, a college classmate, who made some humorous references to the Class Book and prophesies therein as to the future of the man we were now honoring when he was a student at the P. C. P.

Dr. R. P. Fischelis, Mr. O. W. Osterlund, Dr. C. B. Lowe and Mr. Ambrose Hunsberger likewise added their messages of congratulation.

In response Prof. E. Fullerton Cook told of some of his early experiences in the drug store and his association with the members of the faculty of the Philadelphia College of Pharmacy and members of the Committee of Revision. He referred to a recent visit he had made to one of the government departments during which some of the self-satisfaction of the Chairman of the Committee of Revision was brushed down and his ardor at the recent elevation was damped by the reception he had received when he attempted to discuss a pharmacopoeial problem with an official of the departments.

Prof. Cook paid a high tribute to the training and example of his father and mother and to the habits and principles which they had very early grafted into his career and which laid the foundation for the measure of success that had come to him. His association with

Prof. Remington, and especially that relating to the pharmacopoeial revision was invaluable to him as it had given him an acquaintance with the methods of revision and with the personal characteristics of many of the men who were engaged in pharmacopoeial and research work. He appreciated greatly the promised coöperation and unanimity of spirit that appeared to be pervading the entire Committee that had been selected for the tenth revision.

THE DU PONTS TO MANUFACTURE SYNTHETIC CAMPHOR.—Mr. R. M. Carpenter, Vice-President of the E. I. du Pont de Nemours Company, has recently announced that his company has made such progress in the manufacture of synthetic camphor that they are "practically out of the woods," and that this will be of great advantage to all manufacturers of celluloid or similar products. This will relieve the demand for natural camphor for industrial purposes and make it more completely available for medicinal use and should result in a material reduction in the price of the native product.

THE MONSANTO CHEMICAL WORKS ESTABLISHES AN ENGLISH BRANCH.—The Monsanto Chemical Works of St. Louis, Mo., has announced that they have amalgamated in Great Britain with the old established firm of R. Graesser, Ltd., of Ruabon, N. Wales, who were leading manufacturers of phenol and coal tar derivatives. The amalgamated firm will be known as the Graesser-Monsanto Chemical Works, Ltd., with a capital of £400,000 fully paid. The purpose is to continue not only the manufacture of the phenols and cresols formerly made by the Graesser Company but likewise to manufacture in the plant in Wales a full line of chemicals as manufactured by the Monsanto Chemical Works in America.

LEHN & FINK, INC., ANNOUNCE FURTHER BUSINESS ADVANCES.—Mr. Wm. J. Gesell and Mr. Robert Plaut, officials of this drug firm, have sailed for Europe upon a business trip. They will investigate market conditions abroad and secure needed drug products for the American market.

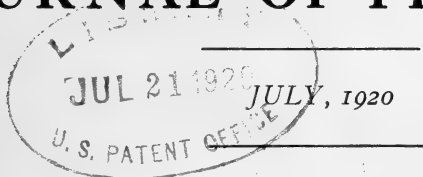
Mr. Edward F. Cunningham is now connected with this firm, paying special attention to the Latin-American field. He expects to spend the summer in a trip to Cuba, Haiti, San Domingo, Porto

Rico and Central American countries, and in the near future he contemplates a business trip to South America.

**THE UNITED STATES IN NEED OF CHEMISTS.**—The Civil Service Commission announce that an examination open to all male citizens of the United States meeting the requirements will be held on July 6th for organic chemists and inorganic chemists. They announce vacancies in the Philippine service at \$3,000 per annum or higher. "The duties of these positions will involve a certain amount of routine work but there will be opportunity for individual research work and appointees must be capable of performing research work." Eighty per cent. will be allowed for education and experience and 20 per cent. for publication or theses to be filed with the application. The applicant must have graduated from a four-year high school course or possess an education equivalent and in addition graduated with a bachelor's degree from a college or university, such degree requiring the completion of at least 118 additional semester credit hours of which at least 30 must have been in chemistry and likewise at least one year of subsequent experience in research work either in graduate work or in a commercial laboratory. By the term semester credit hour is meant one lecture or recitation hour or two laboratory hours per week per semester. The applicants entering for the position of organic chemist must have had training and experience in organic chemistry and those entering for position of inorganic chemist must have had training and experience in general inorganic and physical chemistry. A thesis showing original work or publication of such work must be submitted. The applicant must be under 40 years of age and submit with the application an unmounted photograph taken within two years with his name written thereon. Applications should be made to the United States Civil Service Commission, Washington, D. C.

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# THE AMERICAN JOURNAL OF PHARMACY



## EDITORIAL.

### "THE END OF THE LAW IS OBEDIENCE."

In this issue we publish in full the address of Mr. William L. Crounse on "Alcohol: Its Relation to Science and Industry," delivered before the recent meeting of the American Pharmaceutical Association. In this, alcohol is properly defined as the most important raw material used in chemical and pharmaceutical industries and the responsibilities of the pharmacists under the Volstead Act are clearly set forth.

Equal prominence is likewise given to the account of the Annual Meeting of the Missouri Pharmaceutical Association, prepared by Secretary Whelpley. We would direct the special attention of our readers to the following resolution appearing in this record as adopted at that meeting.

"Believing that the government committed a tactical error in wishing the liquor business upon the retail druggist, we, therefore, do resolve, in the interest of law-enforcement and that the high standard of pharmacy may be preserved untarnished to politely but very firmly decline the 'honor,' standing pat on the proposition that liquor should be distributed through the dispensaries owned, operated and controlled by the government."

This stereotyped resolution has probably been offered before every State pharmaceutical association that has so far held its 1920 meeting and in those whose annual conventions are yet to come, a similar resolution emanating from the same source may be expected to appear.

It is only too evident that after all human nature is not very

different now from what it was on that day when Moses, incensed at the perversion of the tribes of Israel toward idolatry, decried: "I looked, and behold, ye had sinned against the Lord your God, and had made you a molten calf; ye had turned aside quickly out of the way which the Lord had commanded you."

It has always been a favorite method of the extremist, whether he be a rank demagogue or a pure sentimentalist to appeal to the emotional in his audience by high sounding phrases and glittering generalities. Pharmacists have been declared to be as prone to follow some "swan leader" that would pervert them from the straight line of professional duty and service as were the Hebrew children prone to listen to the 'enticer to idolatry' and thereby forsake their deliverer the true and living God of their fathers.

The best test of the validity of any proposition is to subject it to deliberate analysis and so we will dissect the several phrases composing this resolution and present the isolated statements along with the undisputed facts in evidence. The initial phrase, as the premiss, asserts: "Believing that the Government committed a tactical error in 'wishing' the liquor business upon the retail druggist." We note here (1st) 'believing' (2nd) that 'the Government committed an error' (3rd) 'wishing' (4th) 'the liquor business' (5th) 'upon the retail druggist.' Each of these integral parts of the phrase are positive statements entirely unsupported and some of these are at variance with the wording of the law.

We will dismiss the first of these, "believing," as a personal privilege, with merely a comment that it is presupposed that a body of self-respecting and thoughtful citizens in giving public expression to a *belief* have given due consideration to the reasons therefore and to the context assigned as the basis for the asserted "believing."

The second, that "the Government committed an error," whether only "tactical" or otherwise; it may be safely stated that "the Government" is carrying out the mandates of the people as expressed by the adoption of the Eighteenth Amendment to the Constitution and the statutes.

There has been no evidence whatever of any "wishing" but quite to the contrary the law is being *deliberately enforced* in accordance with the provisions of the said amendment and statutes and this, it would appear to us, is the duty of "the government."

The term "liquor business" has been universally applied to the



dealing in intoxicating liquors for beverage purposes. It is inconceivable that anywhere in these United States, it should not be recognized that the Eighteenth Amendment *prohibited* the manufacture, sale, transportation, importation or exportation of intoxicating liquors; that this and the Enforcement Act have outlawed "the liquor business." It is incomprehensible that a deliberative body, such as a pharmaceutical association, especially in Missouri, is supposed to be, would now resolute about a business that the will of the people and the laws of the land had outlawed and even more so that they would even suggest that such a disreputable business was to be by the "Government" "wished" "upon the retail druggist."

The Volstead Act recognizes that the use of alcoholic liquors is necessary for the extraction, solution and preservation of medicinal preparations and rightly provides the means by which the druggists may obtain the supplies required for such uses. Further, that at times, certain distilled spirits and wines are considered by the attending physician as a therapeutic necessity and it very carefully prescribes methods by which the physician may issue prescriptions for these in limited quantities and then very rightly *considering that they are medicines directs that these shall be filled only through a pharmacist "duly licensed under the laws of his State to compound and dispense medicine prescribed by a duly licensed physician."* Is it not the legitimate duty of the licensed pharmacist and of no one else to dispense medicines? Is not this the very basic principle that has justified the enactment of pharmacy laws for the protection of the public against promiscuous and incompetent dispensing?

This is an irrefutable statement of the law and the facts and no perversion will justify an assertion or even an intimation that "the Government" is desirous of providing for a continuation of "the liquor business" or of "wishing it upon the retail druggist."

The second clause the resolve "in the interest of law enforcement," is ambiguous and contradictory and inconsistent in that, instead of upholding the law and its enforcement by the procedure prescribed, it proposes an entirely different method than that provided for. In the language of our title, "The end of the Law is obedience." It is the plain duty of every citizen of this Country to respect and obey the laws. The question here is "law enforcement" as stated and it does not minimize the matter in the least to

adopt equivocal resolves. The people have spoken by Amendment and Congressional Enactment and their mandates must be obeyed alike by the public officers (the Government) and the citizens so long as these remain the law of the land.

The responsibilities and obligations placed upon *the pharmacists* by the Volstead Act are certainly no greater nor more of a hardship than those imposed by the Harrison Antinarcotic Act. We have italicized the pharmacists because we look upon these acts as recognizing professional pharmacy and that the dispensing of all medicines should be by the licensed pharmacists. We cannot doubt that Congress considered the possibility of establishing dispensaries for the distribution of alcoholic liquors. That the conclusion was adverse to such a method is certain. How far the results of the experiments with State dispensaries and the grave danger of abuse deterred from such an action is not known. However, we do not hesitate to assert that under the provisions of the Volstead Act the danger of illicit distribution of liquors will be lessened continuously and that eventually their legitimate prescribing and dispensing as medicines only will be assured.

Let the pharmacists appreciate that if government dispensaries are necessary for the proper dispensing of prescriptions calling for whiskey or brandy that they will equally be necessary for the dispensing of prescriptions calling for morphine or cocaine. Moreover, that such action is an open and broad aspersion of the professional standing of pharmacists and their right to demand the respect and confidence of the public and that they merit responsibility reposed in their professional integrity by this Law. To decline the responsibility imposed upon pharmacists by the Enforcement Act, could not be considered as declining "the honor" but as shirking a professional responsibility. The discharge of a duty in obedience with the law would appear to us as preserving the standard of pharmacy untarnished and far more so than a captious refusal to do so under the misnomer of "declining an honor."

After all, the Mosaic injunction is a safe and worthy advice for the pharmacists to follow:

"According to the sentence of the law which they shall teach thee, and according to the judgment which they shall tell thee, thou shalt do; thou shalt not decline from the sentence which they shall shew thee, to the right hand, nor to the left." (Deut. 17: 12.)

G. M. B.

## REVISED REGULATIONS RELATING TO THE TAX ON TOILET ARTICLES AND PROPRIETARY MEDICINES.

In the June number, we published the preliminary notice of the amended regulations regarding the tax on toilet articles and proprietary medicines and editorially commented upon the same. Under date of June 15th, the Bureau has issued a more extended revision of this regulation and we call the attention of our readers and the trades affected to this later promulgation. It is important that those interested should be well acquainted with the changes in the methods of tax collection made thereby.

The Bureau of Internal Revenue has issued a revised edition of Regulations 51 relating to excise taxes on toilet and medicinal articles under Section 907 of the Revenue Act of 1918. Many important changes have been made in the regulations. Attention is invited to the following which are of particular interest to dealers in the articles taxed under this section:

1. The following paragraphs have been added to Article 5:

"Where a dealer sells toilet water, hair tonics, or other preparations, taxable under Section 907 to a barber for use or sale to patrons, the barber is the consumer within the meaning of the act, and the dealer must affix the necessary proprietary stamps and collect the tax from the purchaser. As to all unstamped articles purchased under certificate, on hand at the time of the promulgation of these regulations, the barber must affix the proper stamp and collect and return the tax when such articles are sold to a customer.

"A dealer, druggist, or person who breaks an original package of a taxable article (1) to use the article or any part thereof in compounding medicines, whether or not on the prescription of a physician, or (2) to dispense any part of the article less than the whole at his soda fountain or place of business, is the consumer within the meaning of the act, and must affix the proper stamps to the original package or container on the basis of the cost to himself, and must himself pay the tax.

"When a dealer, druggist, or person breaks an original package of a taxable article, and sells any part thereof in a separate package or container, as distinguished from dispensing it at his place of business, the purchaser is the consumer and must pay the tax, and the vendor must affix the proper stamps.

"When a dealer, druggist, or person sells a taxable article on a physician's prescription, whether in the original container or not,

the purchaser is the consumer, and the vendor must affix the proper stamps to the container or package in which the article is sold.

"Taxable articles given away as free samples are not subject to tax if a notation is made on the package that the articles is not to be sold for consumption or use, but is a free sample."

2. Article 7 has been rewritten in such a manner that the tax imposed by Section 907 of the act must be computed upon each article sold. Heretofore when one person bought two or more articles at one time, the tax might be computed on the sale as a whole, but a reconsideration of the law showed that this practice was erroneous, and that the tax must be paid upon each article separately.

3. Article 8 formerly held that this tax applied to sales made to the Government, but in the Revised Edition is amended so as to hold that this tax does not attach to articles sold to the United States Government. (This tax is a consumer's tax. But the manufacturer's excise tax under Section 900 applies to sales made to the Government, because that tax is not required to be collected from the consumer.)

4. In Article 9 attention is called to the fact that bay rum, witch-hazel, and shampoo oils and liquids are taxable as toilet preparations: that all toilet soaps, whether medicated or not, are taxable under Section 900, when sold by the manufacturer, and not under Section 907.

5. The following clause is added to Article 14:

"If an article is advertized under a coined word, the exclusive use of which is claimed by one manufacturer or dealer, such coined word may or may not be a trade-mark, but it indicates the distinctive origin of the article and renders the sale thereof taxable, whether it is applied to one or more articles sold by such manufacturer or dealer."

6. The two following paragraphs have been added to Article 16:

"(e) Cough drops sold in packages or cartons having the words 'cough drops,' 'cold tablets,' 'throat lozenges,' 'throat pastilles,' 'troches' thereon, or otherwise held out as a remedy or specific, are taxable under Section 907. Cough drops sold in bulk and held out or recommended as a remedy or specific are taxable. Candy cough drops, such as lemon, lime, and hoarhound drops, sold in bulk by the pound or otherwise, and not held out or recommended in any manner as a remedy or specific, are not taxable under Section 907, but are taxable as candy under section 900, when sold by the manufacturer, producer, or importer.

(f) A preparation, otherwise taxable, is not exempt from tax when it is sold on a physician's prescription, nor when sold in a container upon which the original label does not appear."

7. Paragraph (b) of Article 17 has been rewritten so as to bring out the fact that products whose primary or principal use is a food, as distinguished from medicinal preparations used as a remedy or specific, are not taxable even though held out as having incidental remedial properties, unless they contain a recognized drug and are held out as proprietary medicinal preparations, or as remedies, or as specifics.

8. A clause has been added to paragraph (d) of Article 17 to the effect that serums, vaccines, antitoxins and salvarsan, when prepared by open formulae and advertised only to the medical profession, with labels which indicate use only by the medical profession, are exempt from tax.

9. Paragraph (e) of Article 17 has been rewritten so as to bring out the point that waters, whether medicated or not, produced and sold primarily for use as beverages, although they are held out as having incidental remedial qualities, are taxable as beverages under Section 628, and not as medicinal preparations under Section 907.

10. Articles 24 and 25 have been rewritten in such a manner as to bring out clearly the fact that the tax imposed by Section 907 does not apply to sales made for export; and also, that when articles covered by this section are imported, they are taxable when sold to the consumer in the United States, the same as if they had been manufactured in the United States.

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## LOYALTY TO AND SERVICE IN ASSOCIATIONS.\*

BY E. G. EBERLE, PH. M.

Two years ago I chose as a timely topic, "Loyalty to the Country and to Pharmacy." This time my endeavor is to impress upon myself and others, if possible, the duty of loyal service to associations.

We are often discouraged by imperfections without deriving the encouragement for further application, though fully convinced of the wisdom of the actions concerned; enthusiasm is responsive to interest in work. A traveler was admiring a sunset in the Himalayas,

\* Read before the Pennsylvania Pharmaceutical Association Harrisburg meeting, 1920.

and remarked that it was a beautiful and wonderful world we were living in; a scientist with him was glad of his opportunity in contributing something, however little, to its completion. There is the difference—some are satisfied with conditions as they are, others apply their experience in making progress. These individuals work into the scheme of affairs according to their attitude; their values are inter-related with those similarly engaged, and their worth to the society or the business they are engaged in is dependent on their connection, their coöperation, just as the value of a piece of property is dependent on the surroundings.

Our life—and this includes all the pursuits of life—is what we make it; we get out of it, individually and collectively, what we put into it in the form of energy. For the ardent and progressive worker there is a just reward of wealth to his mind, invigorated with the love of living and doing for others, as also for the advancement of his business and professional activities.

In the discussion of organization plans for pharmacy Mr. Charles G. Merrell presents the thought relative to coöperative endeavor in this way: "No organization or business will be of real value to the community interests that it is intended to serve unless there be born into it ideals and purposes that are not only beneficial to the drug trade but to our national life as well."

The shaping of these activities is not only responsive to our energies and ideals, but on how we impress the public with our coöperative efforts. It is the life of the worker which puts life into his work; the quality is dependent on whether he uses his knowledge only or gives himself with it; his real value develops when he comes in touch with his fellow-men and works into the scheme of affairs in business and industry, and to further this is one of the great purposes of associations. There is reward in doing good work, but, ultimately, success is evolved from coöperation with our fellows, for our good, their good, and the good of those we serve. The development of individuality is a first step; progress results from its adjustment to the individuality of others. To repeat the points briefly, the individual should know himself, his work, and his fellow workers; to become part of an organization is a duty and a privilege. We have within ourselves the capabilities and powers for making pharmacy and the drug business more nearly as we want them to be if our abilities in that direction are more freely exercised.

Loyalty is the basis of association success; the respect and honor

of the people is responsive to loyalty among associates and in so far as this is departed from there is weaker coöperation; the body is open to attack and fails to secure the support of the public which would otherwise obtain. The preferential honor we show to each other, loyalty to ideals, attachment to our profession, business, associations and institutions which make our progress possible are important factors in upbuilding pharmacy and securing the good will of the people. The lack of friendship for one another, belittling the work and inconsiderately questioning the purposes of others, is not conducive to strength. When a member finds a fault his duty is plain—to join with the others in rectifying it.

Dr. Frank Crane recently said: "If you want heart disease, lie awake of nights and listen to your pulse. If you want any member, gland or organ of your physical frame to go on a strike and begin to act up, give it a good dose of self-consciousness. \* \* \* \* \* There is no recipe so infallible for giving you the mulligrubs and the moral pip and the spiritual colic as to keep prying into yourself. Suspect your good impulses and they soon will wither and die. Go around in your soul with a dark lantern, like a Sherlock Holmes, and before long all your decent, self-respecting, manly elements will get disgusted and move out."

So it is with associations—unquestionably we should be dissatisfied with some conditions, but dissatisfied in the right spirit. There may be differences of opinion concerning the advisability of bringing together many who have not the association spirit, who are possessed with the thought that in affiliating they are giving instead of receiving; there can be none among members who have grown with their organization, relative to strengthening the bonds that unite its members for better service in the cause for which they are enlisted. It may be unprogressive not to extend an organization to include all similarly engaged, but it is unwise to smother the enthusiasm of faithful workers. It is difficult for most of us to tolerate the opinions of others when our opinions are of a different cast, and yet, in most instances, we show true nobility of character when we do. At times we may be tolerant when we should not be, but this is seldom true in associations like ours. The spirit of fraternity feeds the aspirations of the sincere and faithful; directs cautious judgment; engenders a fellowship which gives joy to co-workers in the success of their fellows, resents the wrongs from man to man and their calling;

prepares the mind and hand in their field of work for better and more extended service.

This paper may seem out of place at an association meeting where all are imbued with the association spirit, but it is an opportunity for conveying a message of fraternity. The world as never before is tending toward the efficiency of men and utilizing brain and energy in perfecting science and industry; in creating a morale among men and nations. To that end pharmaceutical associations have duties of corresponding importance which should be impressed on the individual pharmacists and inculcated in the profession at large. There is no influence for pharmacy more potent and powerful in the accomplishment of good than that of the business and professional men unselfishly banded together for the purpose of promoting the general welfare of pharmacy, when the paramount thought is loyal service. The growth of coöperation makes for the growth and strength of organization; the importance of the work for which the association is established is measured by the public by the existing morale and the degree of coöperation among its members.

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## THE EXPERIENCE OF A PHARMACIST IN THE WORLD WAR.

BY LUTHER A. BUEHLER, PHAR.B.,

PHILADELPHIA, PA.

Shortly after the outbreak of the war, I enlisted in the Medical Corps, entering that arm of the service for the reason that it is the branch for which a pharmacist is best fitted. University of Pennsylvania Base Hospital Unit 20, the command to which I was attached, was organized as a Red Cross Hospital. We were mustered in at the armory of the First Pennsylvania Cavalry and shortly thereafter the enlisted men were divided into small detachments and despatched to different hospitals throughout the city for instruction. The clinical laboratory detail to which I was attached was sent to the University of Pennsylvania Medical School for a short, intensive course of instruction in bacteriology, parasitology and blood work.

From Philadelphia we went to Camp Merritt, purely an embarkation camp, there going through a series of inspections. We



left Hoboken on the Vaterland, landing at Brest on her maiden voyage into that port. After spending four days at Pontenezen Barracks, in mud and on half rations, we were packed in third-class French coaches; eight men and packs to a compartment, each given a load of bread, a can of corned "wiley" and "gold fish" and told to work out our own salvation for the next three days. Chatel Guyon, the village in which we were stationed, is a mountain summer bath resort in the central part of France, about thirty kilometers south of Vichy, the second largest hospital center in the A. E. F. This district of France known as Auvergne, although the center of the lace and wine industry, by reason of its geography is probably the least progressive part of France, and the only part that has never suffered invasion. Oxen are used for dray purposes; what grain they raise is cut with a cradle and on one occasion I saw threshing with a flail.

It may not be inappropriate to say a few words in regard to the French people as we knew them—by living and working with them, learning their peculiarities, their depth, manners and customs. I am certain the impression which the doughboys (who constitute the major portion of an army) received was not representative of France, for their minds became so thoroughly impregnated with the abominable conditions existing in the devastated areas, that they cannot view France and her people in the true light.

The buildings that we took over were hotels that had been occupied by French Colonials. The laboratory personnel consisted of two medical officers; an enlisted man who had considerable experience in serology; another who assisted in conducting post mortems; a third, whose work was confined solely to clinical photography, and myself. Sterilization of glassware, the care of animals and the policing of quarters was done by convalescent patients and German prisoners.

The first five weeks of the entire staff were devoted to the installation of apparatus and carpentry; in the latter the two officers, both majors, pitched in and sawed and planed and hammered with the men in dennims. Up to the signing of the armistice, work seldom ceased at retreat but was of necessity carried far into the hours of the night and early morning.

I might cover briefly the stages a patient passed through before reaching us. Except during a drive, patients are never sent direct from the front to a base, a week generally elapsing before their ar-

rival. When a man is wounded on the field he is picked up by the regimental stretcher bearers and carried to the first-aid dressing station, which may be but a stone's throw to the rear in any available shelter such as a dry shell hole or within the remaining walls of a shattered building. The dressings that are applied are intended primarily to arrest the flow of blood and bind up the wounds sufficiently for the man to be transported to the Field Hospital. This is back of the artillery, just beyond the range of enemy fire. Wounded are then transferred to the Evacuation Hospitals and mobile organizations farther in the rear. These organizations, moving forward or receding with the line, although their facilities are limited, perform every type of operation, among the commoner ones being amputations and transfusions.

Wound bacteriology is a development of the past war and represents the work primarily of the French. Gas gangrene, which was prevalent during our Civil War, ran its course unchecked until the exact nature of the organisms infecting wounds was learned, this being in the second year of the war. With the knowledge that the grave septicemia from war wounds was due primarily to two groups of bacteria—the streptococci and the gas producing—there developed the Carrel-Dakin solution and surgical intervention. Our routine procedure in the culture of wounds was to send to the operating room, empty, sterile, capillary pipettes or sterile swabs immersed in several Mils. of neutral bouillon. The pipette was filled or the culture media inoculated with the exudate of the wound during debridement and returned to the laboratory. Five subcultures were subsequently made. The first was dextrose bouillon for all aerobes; the second, plain bouillon overlaid with a layer of oil, previously boiled and rapidly chilled, for anaerobes; third, dextrose agar, overlaid with oil, to observe colony formation and gas production; fourth, litmus milk, the ideal media for gas producing anaerobes; and fifth, an agar plate of whole defibrinated human blood for hemolytic bacteria. After eight hours of incubation, a report, sufficiently complete to determine the mode of treatment, could be generally sent the ward surgeon.

The flora that wounds present is very great, every organism of the gastro-intestinal tract being represented. The characteristics of a gas infection are the nauseating odor, the formation of bubbles of gas in the exudate upon the application of slight pressure to the surrounding parts, accompanied by a crackling sound. Any ar-

ticulation that the hemolytic streptococcus has invaded may be considered as irretrievably lost and any bone tissue it has touched will for months and years carry traces of the infection. Nasopharyngeal cultures for the hemolytic streptococcus, of the officers, nurses and ward masters, all those having occasion to dress wounds, were taken at frequent intervals.

When the wound no longer discharged freely and there were indications of granulation, smears were taken at intervals of several days to determine the average number of organisms per field. When this figure did not exceed five it was safe to attempt suture, however, under no circumstances should a wound be closed showing the presence of streptococci. We prepared a limited number of autogenous vaccines from wounds. Their use has not been very extensive.

Located among the hills under fairly ideal climatic conditions, our organization was selected as a center or clearing house for gassed patients and tuberculosis suspects. A man who is severely gassed develops into the clinical picture of tuberculosis and the treatment is practically the same. So great was the number of specimens of sputa submitted to the laboratory that we were compelled to limit the number to be examined daily to fifty. Ten specimens of each patient were submitted; if no tubercle bacilli were detected in that time, no further specimens were submitted for thirty days. A positive report automatically placed the patient in Class D—those incapacitated for any further service in the A. E. F.

During the winter we generally had a half dozen or more cases of clinical diphtheria in isolation, none ever proving fatal. Like everywhere, the culture and isolation of carriers is a problem. Three cases developed simultaneously among two hundred Bosche prisoner convalescents who were quartered in a barn. At that time it would have been impossible to take that number of cultures, therefore the only ones cultured were those having inflamed areas in the throat.

Sporadic cases of epidemic cerebro-spinal meningitis developed from time to time, the majority proving fatal. Our routine procedure in the examination of spinal fluid was to make a Pandy test for globulin; a leucocyte and differential leucocyte count; cultures for pneumococci on Löffler's blood serum; for streptococci on dextrose agar, and for meningococci on dextrose sheep's serum agar. A Wasserman test was also made. The culture of contacts was a much greater problem than in diphtheria, satisfactory cultures being

obtained only when placed in incubator temperature immediately after taking. A case developed at an aviation camp, twenty kilometers to the south of us. It was necessary to transport the 300 men to the laboratory to be cultured.

At this same aviation camp there was an epidemic of Vincent's Angina or as generally termed, Trench Mouth. However, it bears no relation to the trenches, it probably being no more prevalent on the firing line than in the Service of Supply. The lesions which occasionally resemble secondary specific patches are very painful and may be found in any part of the mouth or pharynx. Smears show the presence of a long slender fusiform bacillus and a spiral organism having three to twelve undulations. The latter are best observed in a dark field.

Dysentery was widespread throughout the A. E. F., it being almost as prevalent in the S. O. S. as in the Advance Zone. However, the number of positive cultures and agglutinations was remarkably low. Frequent cultures were made of the water, milk and food supply and the hands of cooks and kitchen police but in only one instance were organisms of the typhoid-colon-dysentery group isolated.

While I have no exact data on the influenza and pneumonia cases in our organization, the number was comparatively small. The several thousand patients and hospital personnel being distributed among some twenty isolated buildings in the hills, coupled with stringent preventative measures, enabled a maintenance of the upper hand and control of the epidemic. The nursing and medical attention were equalled by few civil institutions. These cases involved considerable clinical laboratory work, *viz.*, leucocyte counts, blood cultures and typing of the urine and sputum. White mice were unobtainable for grouping the pneumococcus, therefore the Avery method was employed.

Great difficulty was experienced throughout France with natural amboceptor in guinea pig serum, this condition being met with very seldom by workers here in the States. As high as four consecutive pigs have been killed or bled from the heart, finding that the especial complement was in itself capable of producing hemolysis, therefore rendering it unfit for use in the Wasserman technique generally employed. The inadequate supply of guinea pigs was a great problem, they being furnished by the Bureau of Farms and Gardens of the American Red Cross, located in the Paris district.

The fortunate location of the laboratory in the dispensary and specialty building enabled the attending surgeons personally to use the facilities of the laboratory in many instances. We had the heartiest coöperation and support of the ward surgeons and the extent of the work done reflects their interest in this side of the patients' care and treatment.

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### AS IT WAS IN 1870.\*

BY H. V. ARNY, PH.M.

This auspicious occasion, the Golden Anniversary of the oldest State pharmaceutical association from the standpoint of continuous operation gives us the opportunity to rejoice and to remember. The writer is one who believes that the future is built upon the past and while too much delving into history may make a man as dried up as a mummy, enough makes one the better for the delving.

So let us lift the curtains of the past and let us see what the pharmaceutical journals of 1870 said about 1870. As to the New Jersey Pharmaceutical Association we find three references noting the meetings in Newark on Jan. 26, Feb. 17 and 24th and in Trenton on March 24th, when the proposed pharmacy law, following a "model" draft approved at the 1869 meeting of the A. Ph. A. was drawn up and ordered presented at the next session of the legislature. The Proceedings of the American Pharmaceutical Association for 1870 states that at its Baltimore meeting the delegates appointed from the New Jersey Association were Randall Rickey, J. L. De la Cour, Jr., William Rust, E. F. Kelly and Julius Fehr. Of these only the first named was present at the meeting. In that year New Jersey had 28 A. Ph. A. members, seven from Jersey City, three from Camden, two each from Newark, Burlington, Morristown, and one each from Bordentown, Elizabeth, Elizabethport, Hackensack, Hoboken, Madison, Mt. Holly, New Brunswick, Plainfield, South Amboy, Trenton and Vincentown.

This is all of the 1870 references to the New Jersey Pharmaceutical Association, more space being given to the West Virginia and Indiana associations, both of which died after a few years, while our association has lived and grown and flowered even unto this, its Golden Anniversary.

\* Read before the New Jersey Pharmaceutical Association, Newark, N. J., June, 1920.

The next important item of news is the Pharmacopoeial Convention of 1870 at which no delegates from New Jersey were present and at which time there were elected to the Committee on Revision the distinguished pharmacists, A. B. Taylor, Maisch, Ebert, J. Faris Moore, Markoe, and Wenzell.

As to colleges, we note that New York had eleven graduates at its commencement, Massachusetts six, the University of Michigan, twenty-eight Ph.C.'s, and Philadelphia, fifty-one Ph.G.'s. We also note that Chicago and Louisville announced the opening of their colleges in the fall of 1870. No published record was noted of other colleges, although several others were in operation.

The pharmacy course at the University of Michigan was then in its first years and was viewed with disapproval by the "old line" colleges. At the A. Ph. A. meeting, in his presidential address, E. H. Sargent of Chicago discussed the matter and stated "a feature complained of and one likely to create trouble hereafter is that a student may be graduated as a Master in Pharmacy without having any experience whatever in the practical work of the shop, thereby unsettling our notions as to what constitutes a pharmacist." The phrase "unsettling our notions" is a gem. How many things against which our orators rave as destructive are merely matters "unsettling our notions."

Among the "new medicines" of 1870 we find many papers upon chloral hydrate; phenolsulphonates as "wound dressings" (the word "antiseptic" is met but seldom); phenol and its preparations; eucalyptus, as an antiperiodic; bromoform; and potassium permanganate for snake bite and as a deodorant. One enthusiast gives permanganate internally using raspberry syrup as vehicle! Two new remedies that have not stood the test of time were a tincture of pole cat glands recommended for asthma and the sniffing of fresh sea-weed for hay fever.

Among the "new preparations" of a half century since we find liquid pepsin and pepsin wine (Schaeffer's classic paper on the subject appearing that year) "dragees" and granules; hypodermic solutions; granular, effervescent, magnesium citrate; elixir of iron, quinine and strychnine, which was subject to much criticism; fluidextracts, especially their preparation by percolation, a paper on the subject by Campbell being widely discussed; compound elixir of taraxacum, Candidus recommending it as a vehicle for quinine; glyconin; and cod liver oil creams, the forerunners of our present emulsions.

The popularly prescribed proprietaries of 1870 were evidently Chlorodyne, and Battley's Sedative, judging from the papers discussing imitations of these products. In those days as always, a popular nostrum by imitation, became an accepted galenical, even though there was no National Formulary in which to place it. In that year appeared Chandler's classic report on his analysis of the then popular cosmetics.

In pure science, we find Wormley's classic paper on the alkaloids of gelsemium, with the wonderfully wrought illustrations of his wife, which were so exquisitely delicate that no commercial engraver could do them justice and she learned the art of engraving in order to prepare the plates herself; H. C. Wood's paper on the therapeutics of veratrum alkaloids and lastly an address given by William Hope, before the British Association on the "new germ theory of disease."

In technical science many things now considered as everyday matters, subjects in which millions of capital are now invested, were then considered as new and in their experimental stage. Among these undertakings we find the introduction of beet sugar culture in the United States, the canning of meat, "the tinned Willy" of A. E. F. memories; safety devices in the petroleum business, notably the fixing of the "flash point;" the manufacture of glucose and of artificial ice; the development of natural gas wells in certain sections of New York and at Erie, Pa.; the production of oxygen upon a commercial scale; the financially successful manufacture of aniline dyes, this being the topic of a notable paper by Perkin, the discoverer, in 1856, of mauvein, the first coal-tar dye stuff; and the use of naphthalin as a moth expeller.

And lastly, in the domain of political economy, we find a note that presages good news for us in the "Sweet Bye and Bye." It is stated that by the Law of July 14, 1870 the Internal Revenue War Taxes were to be lightened; that this would mean that the American public would be relieved of the staggering burden of \$55,000,000 per annum.

Such is the record of 1870, a record upon which the historian could dilate until his audience was asleep; for almost every topic cited above has much that is interesting to discuss. Surveying the work of 1870, one wonders whether the historian of 1970 talking about 1920 will be able to find as much that has stood as well the test of half a century as have many of the new things of 1870. The year of grace 1870 was a good year and one of the best things accom-

plished that year in a pharmaceutical sense was the founding of this association which we are so proud to honor at this its semi-centennial.

In closing acknowledgments are due to the *Proceedings of the American Pharmaceutical Association*, the *AMERICAN JOURNAL OF PHARMACY*, *The Druggists Circular*, the *Pharmaceutical Journal and Transactions* and *The Chemist and Druggist* for 1870 from which the facts given in this paper are collated.

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## THE USE OF DRUGS IN DISEASE.\*

BY R. G. ECCLES, M.D.,

BROOKLYN, N. Y.

To how many of your minds has the idea come that pharmaceutical chemistry may be the oldest profession on the earth? The very first of living things must have started as a drug compounder. As soon as the early Protozoa began colonial life—*i. e.*, when they changed from one-celled to multi-celled organisms—they must have exchanged with one another those kinds of drugs now known to physiologists as hormones. With progress upward to the higher forms of life we find, on study, that the exchange of drug commodities increased very greatly. Myriads of substances unknown to the lower forms appear among the higher. Prof. Huxley, the great English biologist, of the end of last century and the beginning of this, declared that of the many millions of organic substances produced by plants and animals they are all combinations of exactly the same elements as are found in “smelling salts” with a trifling amount of mineral substances. Out of these the cells—the primitive pharmacists—produce by their compounding almost the entire array of organic substances found upon your shelves labelled with what laymen look upon as hieroglyphics. While most pharmacists know, in a general way, that the great bulk of their medical supplies are the products of these ancient pharmaceutical chemists few have stopped to consider the fact that their own bodies are miniature drug depots, and, that a quite respectable proportion of the drugs found therein vary but slightly from those they sell every day over

\* Read before the Fiftieth Annual Meeting of the New Jersey Pharmaceutical Association, Newark, June 8, 1920.



their counters. The same identical radicals are found in them as are found in the store stock. Your bodies' cells have been licensed by nature, after a proper training in the nature of drugs, to put up the claim that within their membrane walls "Prescriptions are Carefully Compounded." Within their walls they are constantly at work filtering, precipitating, dissolving, macerating, digesting, percolating, oxidizing, reducing, and hydrolyzing. An inventory of the kinds of goods they carry—not ready made, however, but as chemical radicals—would be astonishingly like those found in a Jersey pharmacy. There are in the cells of a normal human body material radicals for the production, on demand, of some very potent compounds but all so cared for as to be quite harmless. Let us, for a moment, look over part of the list as it occurs to us at first thought. There is phosphorus, phosphoric acid and phosphates; iron, iron oxides, sulphides, sulphates and carbonates; sulphur, sulphides, sulphates, sulphites, sulphurous acid, sulphuric acid, and sulphuretted hydrogen; ammonia, ammonium carbonates, sulphides, sulphates, sulphites and phosphates; nitric and nitrous acids with a host of nitrogen salts, t. n. t., nitroglycerin and dynamite; hydrocyanic acid, cyanogen, cyanates and cyanides; iodine, iodides, iodates, and thyroidine; arsenic acid, arsenic, arseniates and arsenides; formaldehyde, formic acid, formates and many polymers of formaldehyde; glycerine and a host of different kinds of tryglycerides; hydrochloric acid, chlorine and a multitude of chlorides; calcium, calcium chlorides, carbonates, sulphates, sulphides, and a multitude of organic calcium compounds; unnumbered substances carrying the benzol ring; fluorine, hydrofluoric acid, and fluorides; alcohol, acetone, acetaldehyde, acetic acid, and acetates of many kinds; citric acid and citrates, oxalic acid and oxalates, oleic acid and oleates; potassium and its salts; sodium and its salts; silicic acid and silicates; copper and its salts; manganese and its salts; etc. In amido-valerianic acid there is the radical for production of valerianic acid and valerianates. The nucleic acid contains the raw materials of phosphorus, phosphoric acid and phosphates, hydrocyanic acid and cyanides, as well as of glucosides. The proteins hold in their structures three amino acids that contain the benzol nucleus, namely phenyl-alanin, tyrosin and tryptophane. These are the mother substances of carbolic acid, benzoic acid, salicylic acid, benzaldehyde, aniline and numerous aromatic substances that perfume our drug stores, to say nothing of malodorous skatol and indol. These three

amino acids are found in every cell of the human body but are particularly abundant in hair and nails, skin and mucous membrane. Every tissue that is exposed to infection by parasites, to an unusual degree, contains more than those not so exposed. They, with cystin and cystein, that contain oxidizable sulphur, are, strange to say, the first of the amino acids released by trypsin in the bacteria laden intestine. There they produce the well-known antiseptic substances named and particularly carbolic acid. There the danger of having the cell-foods—the amino acids—stolen by saprophytes and parasites is greatest for these organisms subsist and fatten, as do the cells, on these amino acids. The oxidation of cystin, by bacteria, produces sulphurous acid an antiseptic about as powerful as carbolic or benzoic acids which it fortifies. It seems as if nature had set a trap for the parasites by which they injure themselves as a cheese-set trap catches mice. Meats, fish, eggs, milk, gluten, and the like, all contain an abundance of these bacteria-inhibitors that only act when being digested or putrified. The odor of skatol in putrid food is evidence of the fact that the bacteria are, by their deprecations, producing antiseptic substances to inhibit their activity. The tyrosin is abundant in melanins, the pigments of the negro's *rete mucosum*, the choroid coat of the eye, and in the hair. With the approach of old age the hair turns gray, the nails brittle, and the eye-sight dim because of a shortage of tyrosin and its oxidizing enzyme, tyrosinase. Skin affections also increase as melanin diminishes. The black skin of the negro accompanies his relative immunity from yellow fever, malaria and trypanosome disease as compared with the lack of immunity in white men. Darwin has pointed out that certain skin diseases of animals attack only unpigmented ones, leaving the pigmented untouched, while piebald animals are attacked only on white spots. The shortage of tyrosin seems to be responsible. Millions of years ago the phenylalanin and tyrosin of plants was buried in the ground with the plants that produced them. We now dig them up as coal and the aromatic radicals of these amino acids constitute the antiseptic substances of coal tar. Our beautiful anilin colors and our many new synthetic remedies have come from these. Their antiseptic power have preserved them for all these years from the deprecations and ravages of time. We, too, like coal, derive our antiseptic radicals from plants as no animal seems to possess the power to produce them, in spite of the fact that none can live without them.

Among the first of well-known men to proclaim the virtues of these substances, as found in coal tar, was George Berkeley, Bishop of Cloyne, Ireland, who died in 1753. You have all, no doubt heard his prophetic slogan, that has become a household expression: "Westward the course of Empire takes its way." You probably also know that California has honored him by calling the university city of that State by his name. He extolled tar water as a panacea for many ills and this, together with his then unpopular philosophy, brought ridicule upon him. Pope, the great English poet, however, came to his defence and in one poem says:

"Truth's sacred fort the exploded laugh shall win,  
And coxcombs vanquish Berkeley with a grin."

His supposedly erratic defense of tar water has been vindicated by modern research and the scriptural claim, that "The leaves of the trees shall be for the healing of the nations," is also vindicated. In these leaves are, and always have been, produced the world's supply of the best known paracitisides and antiseptics. All of our food proteins are leaf products, so far as they contain phenylalanin and tyrosin, as are also all coal tars, so far as they contain the benzol nucleus. Through this discovery we are but beginning to see that throughout living nature a battle with parasites is going on in which these constitute the implements of war. To successfully vanquish individual diseases we must pursue the methods of nature in the way it holds in abeyance the countless millions of actual and potential disease-producing parasites that menace all other living things. The way she controls disease we must control it, and the weapons she uses against microbes we must use, in order to be successful. Fifty years ago little was known of these invisible foes and a century ago only the larger parasites had any place of recognition in our textbooks of medicine. Now we have discovered them to be the constant enemies of every thing that lives. There are now catalogued from 5 to over 20 different kinds for each particular species of plant and of animal. Over sixty have been catalogued and named as enemies of the oak trees. Not a single soul within the hearing of my voice is, at this very minute, free from them. We are all disease carriers. Streptococci, staphylococci, pneumococci, and *Bacillus coli communis* are now waiting upon, and within our bodies, for some favorable opportunity to start disease. They are being held at bay by the antiseptic substances we have named as present in skin and

hair, mucous membrane and nails. A scratch of the skin may inoculate the apparently trifling wound with some virulent kind of streptococcus that starts erysipelas and kills us. We stop its multiplication by a free use of exactly the same radicals as the skin that was removed contained. Our supply, however, most likely came from coal tar in which it had lain for many milleniums since the plants that produced it were menaced by still other kinds of parasites. With the advancement of bacterial and chemical knowledge we are, as such cases show, getting rid of empiricism and discovering broad, general laws of treatment that are as sound to-day as they were when, in the Carboniferous era, these substances were formed. Unfortunately, there are among us a large number of people who measure progress by the yard-stick of their own ignorance. Knowing nothing of discoveries that lie outside of their studies they look, with unfeigned terror, on any kind of change that does not correspond with the opinions of their great grand-dads. They cling to old fads and fancies as they do to truth when they happen to possess it. Not laymen alone are guilty of this folly. It is quite common among physicians and pharmacists as well. We are all loath to give up ideas that we took in when babes and sucklings. We have little of the bravery of the pioneer, and dread, with undisguised fear, every innovation that collides with our early impressions. Medical science has entered a new path since our discovery of the cause of disease and we are now being called upon to remodel our ideas in respect to processes of cure. In the confusion that is resulting from this change we are witnessing an intense conflict of opinion between progressive and sessile, or conservative, minds. Remarkable as is the fact, too, the conservatives have chosen for themselves the title "reformer" as they seek, with might and main, to reform things backward.

Among the new so-called reformers are those who seek to stop the use and manufacture of vaccines, those who oppose research in physiology and therapeutics, calling the processes pursued by the name of vivisection and themselves antivivisectionists, and those who oppose all drug treatment and condemn it as wholesale poisoning. The creed of the latter is that all drugs are "deadly" poisons and all administration of drugs as poisonings. From their point of view poisons are poisons inherently, and it matters not whether the dose is large or small it poisons in proportion to the amount given, the result being cumulative. This, of course, is a very old

notion as well as a very false one, if we can rely on the experimental evidence of modern science. This view, however, has during the last two decades made immense progress in the minds of both laymen and doctors. It has built up a host of therapeutic nihilists, who want to "cast physic to the dogs," and is the foundation inspiration that leads to the doors of the Christian Science church. It was the inspiring thought among those who demanded the abolition of the use of alcohol in every possible form. It is instigating a crusade against the use of tobacco, tea, coffee, etc. Can you not see where this sort of logic is travelling and what the final result is likely to be unless we can educate the mass of voters to alter their views, in some safe degree, in this craze? Should these emotionalists increase in numbers as fast in the next century as they have done in the past what is likely to happen? Would it astonish you much if, when they feel that they are strong enough, they should raise the cry of "Stop Poisoning the Sick?" They would have no trouble in finding, in medical literature, an abundance of thoughtless utterances, of able medical men, to confirm their contention and win votes enough to close drug stores as they have closed saloons. Take for example, these two statements, one from *Bulletin 30* of the Committee of One Hundred on Public Health, p. 88, and the other from a State Board of Health *Bulletin*, as a statement from a leading medical college professor of New York:

"It would scarcely be an exaggeration to say that the first rule of hygiene is to avoid poisons."

"'ALL POISONS.' All of our so-called curative agents (drugs) are poisons and, as a consequence, every one diminishes the vitality of those who take them."

These views are an echo of the time when men conjured out of their inner consciousness what they called truth. An appeal to nature by actual experiment would quickly have convinced them that so far are they from being true that, under proper qualification, the very reverse is declared by nature to be true. Not one of those who make statements like these has any knowledge of what a poison is or why it poisons. It does not occur to them that among the most poisonous substances known to man are such foods as beef, chicken, fish, egg, breads, and proteins generally. Notwithstanding their poisonousness we could not live unless our food contained them. In the *Journal of Infectious Diseases*, Prof. H. G. Wells, of Chicago University, tells us that when egg white, in a perfectly pure condi-

tion, is injected into a rabbit's circulation, in two intermittent doses, very minute amounts kill. He says: "One fifty-thousandth of a cubic centimeter of a solution containing but one-millionth of a gram of protein (egg albumin) sensitizes fatally." (Oct. 20, 1908, p. 456.) That certainly beats strychnine. When these food substances are taken by the mouth the digestive fluids convert them into amino acids that are perfectly harmless. If they enter the circulation partly digested fatal results occur from what is technically known as anaphylaxis. It is now believed that all the various symptoms of different kinds of diseases are due to the anaphylactic poisoning of the body substances by the dead parasites that are being digested in the blood stream. A poison is, so far as we at present know, a substance that has an affinity for some of a cell's molecules and that by union with such molecules produces fatal disturbances in metabolism. The cells are all surrounded by specific membranes composed, as now believed, of protein-like substances. Injury to these, by union with chemicals that damage their function, alters their semi-permeability and leads to cell-death. Egg-white is broken up in the circulation into relatively large molecules of what we may call polypeptids and these have different affinities for different cells but are too large in size to take a proper place in metabolic changes. They act like a monkey wrench thrown between the cog-wheels of a machine. Meat, when partly broken up, has an affinity for a different set of cells from that chosen by egg-white fragments. Fish has still another set of such affinities. The proteins of microbes have, under the same circumstances, still other attractions for different cells and each kind of microbe poisons, with its protein fragments, different kinds of body cells. Hence different diseases display different symptoms. These microbe proteins, so far as we know, behave, when fully digested, exactly as do meats, fish, and eggs—they nourish our bodies. Only at a certain stage of partial digestion are they poisonous. The most deadly toxins of disease have been fed to animals by the mouth, in relatively large amounts, without a sign of poisoning. They are digested into harmless and nourishing amino acids. The toxins of botulism is an exception that is probably composed of molecules sufficiently small to be able to pass into the circulation undigested and, therefore, able to produce anaphylactic poisoning. The deadly cyanogen glucosides behave in a similar manner to proteins but they are not digested by the enzymes of the blood if introduced hypodermically. In the alimentary track

hydrocyanic acid is released as a poison. In the circulation none of the cyanogen seems to be released and all of the molecules, in reasonable amounts, are removed by the kidneys. These glucocides, therefore, behave in an exactly reverse manner, so far as their poisonousness is concerned, to that of the food proteins.

All so-called poisons appear to possess specific affinities for different kinds of cells just as do the poisons let loose from foods in anaphylaxis, and these are but particular cases of the general rule in all food substances. The bone cells attract a large share of the lime of the circulation. The liver cells take up most of the free sugar and deposit it as glycogen. The thyroid cells take charge of most or all of the iodine. The cells of the choroid coat of the eye drag in a large share of the melanin. In the same way the nerves that supply the extensor muscles accumulate lead and produce, thereby, wrist-drop. The neurons of central vision have an affinity for something in tobacco that leads toward dim vision and blindness. Horses that have fed on tobacco leaves suffer, because of this, from amblyopia. Methyl alcohol breaks up, in the circulation, into something that acts on these same neurons producing blindness. Digitalin and aconitine act particularly on the heart muscles. Curarine acts on the termini of the motor nerves. Adrenalin acts on the terminations of the sympathetic fibres. Caffein has a particular affinity for the kidney and muscle cells. Formaldehyde by linking itself to the aminogen groups of the protein is supposed to arrest metabolism. Ether, chloroform, cocaine, morphine, codeine, and heroine have an affinity for lipoids, being soluble in them, and through this solubility are thought to be able to act on the nerves of sensation, stop their functioning, and abolish consciousness of pain, locally with some and generally with others. In quite small amounts these substances all seem to have but a slight stimulating effect upon the cells that they reach and act upon. A judicious use of digitalis, or of digitalin, strengthens the heart muscles to which they appear to be attracted. A similar use of atropine or belladonna tones and strengthens non-striated muscles, stimulates the respiratory centers and increases intestinal peristalsis. Strychnine is attracted to, and acts upon, the vaso-motor and motor centres of the cord, thus increasing the circulation and producing thereby a general tonic effect, through increased supply of arterial blood. These, and all other so-called poisons, when given in proper amounts, act upon special parts of the body—not to injure them—but to increase their physiological tone.

When animals, and even unicellular organisms, are exposed to them they acquire immunity to their toxic effects, to a most extraordinary degree. Prof. Roger, in his "Medical Pathology," states that an amoeba "can be gradually habituated to water containing 2 per cent. of sea salt; it becomes so accustomed to the new conditions that it perishes when again brought back into ordinary water" (p. 79). Parks, in his work on "Pathogenic Bacteria," tells us that bacteria can be habituated to carbolic acid, if administered in sufficiently dilute solutions, so that, in time, they are able to use it as a food (p. 26). Kobert, in his "Practical Toxicology," says: "The smallest snail will withstand more strychnine than an adult man. Many of the stronger cardiac poisons have no action whatever on insects. The rabbit can take more morphine than can a man fifty times the animal's weight. Doses of lead, nicotine, cysticine, etc., sufficient to poison man fatally do not injure the goat. Amygdalin does not affect dogs, but it kills rabbits. The hedge-hog takes with apparent enjoyment a dose of cantharides that will kill several persons under excruciating pains. Whereas, the frog is extraordinarily susceptible to the digitalis poisons, they have no effect upon the toad" (p. 5). The mongoose is not affected by a snake bite. The California oil fly develops in crude petroleum oil. Prof. C. Pichet has shown that in such cases as he has studied "The law is established that in simple analogous substances toxicity is increasingly greater as the substance considered is found the less abundantly in nature" (*Chem. Abs.*, Feb. 20, 1911, p. 714). Habit in the use of the poisons, like habit with arsenic, alcohol, morphine, tobacco, etc., probably has something to do with such effects. The cells are toned up to a new standard. In vaccination, and serum treatment of disease, the stimulation of cells leaves them able to resist greater amounts of the toxins of such diseases. The anaphylactic effects of different proteins and the susceptibility to most kinds of diseases vary with experience. After one attack of typhoid fever the second attack, if it comes at all, is likely to be very much milder. The cells become more resistant. Prof. H. M. Richards states that: "It has been established that many, if not all, classes of substances which exert a toxic action on protoplasm will become stimulating if presented to the cells in sufficiently small doses" (*Nature*, March 24, 1910, p. 115). Prof. Pfeffer, in his "Physiology of Plants," says: "Submaximal doses of many and perhaps all poisonous substances accelerate respiration, growth, and the production of heat" (Vol. I,



p. 264). Prof. Davenport, Director of the Department of Experimental Evolution, of Carnegie Institute, reporting his many experiments with poisons on plants, says: "It is clear from this table that the addition of even small quantities of innutritious and poisonous substances may so affect the hylogenic processes as to cause twice, or even far more than twice the normal formation of dry substances in a given time, and that this excessive growth increases with the concentration of the poisonous substances up to a certain optimum beyond which growth declines again to below normal" (*Proceedings A. A. Advancement of Science*, 1907, p. 504).

Without the subtoxic effects of adrenalin on the circulation the arteries could not function normally and without thyroidine, growth is arrested and health seriously impaired. Without hydrochloric acid how would gastric digestion proceed? In such cases it is evident that what we call poisons have a very important place in physiology. There is a universal law seen in all living things. It is the benefit derived from normal effort, normal heat, normal electric currents, and normal chemical stimulation. Within proper limits all of these are beneficial. It is only when their stimulation exceeds such limits that they become harmful and this harmfulness is evident in all of them. The muscles are strengthened by massage and by effort. The skin of hands and feet thicken with work. Heat, in proper amount, favors growth as toxic substances do. Just as digitalis strengthens the weakened heart so all poisons strengthen such parts of the organism as they act upon, provided, of course, that the physiological maximum is not exceeded. When will the world take to heart this lesson and use it for our benefit? When will we all learn that a sick man is always a poisoned man? The anaphylactic effects of the poisons of typhoid give us the clue to the particular parts of the system that need toxic toning against such poisons. The anaphylactic effects of malarial poisons give us a similar clue to the parts of the system that require toning against these poisons. When we know enough to experimentally follow these clues, for all sorts of diseases that we suffer from, and that kill us, we will know how to do by every one of them as we do now with digitalin in weakened heart. Such knowledge will put us on the way to true prophylactic medicine.

To know how, during threatened epidemics, and at other times, to strengthen every susceptible cell against that particular kind of disease, will be to enter into a new era of preventive medicine.

To-day we are "locking the stable door when the steed is stolen." Then we will be locking the door before the thief can enter. Our present efforts in preventive medicine have wrought miraculous results but they are all centred upon environmental prevention. If "an ounce of prevention is worth a pound of cure" in one direction it should be in the other. Nature is showing us many ways by which to resist the poisons of microbes. Let us learn our lesson from her. We must become able to poison our poisoners and to inhibit the effects of their poisons upon our cells. The druggists have a duty here that is as great as that of the doctor. He should discourage all reckless talk about the poisonousness of drugs by teaching his customers, when he has an opportunity to do so, that there are no such things as poisons *per se*, that strychnine, in proper physiological amounts is no more a poison than is bread or meat, egg or cheese, and that soluble poisons, properly diluted, are more likely to be beneficial than harmful. Unless this is done there may, at any time, arise a wave of ignorant hysteria that will destroy—as it has already hampered and hindered—medical science in its work of aiding the deluded men and women who are sponsors for restricting and troublesome laws.

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## A NOTE ON THE EXAMINATION OF A COMMERCIAL SAMPLE OF OIL OF PENNYROYAL.\*

BY GEORGE M. BERINGER PH.M.,

CAMDEN, N. J.

On two occasions, recently, samples of what, it was reported, had been sold as Oil of Pennyroyal were presented to the writer with the request that he determine first, whether the sample was Oil of Pennyroyal, and secondly, if it was unadulterated. The sample referred to in this note was one of these.

The sample measured only 15 Cc., and it was desirable to retain at least a portion in the original container for court evidence, so the quantity available for examination was not large.

The U. S. P., 8th Revision, defined *Oleum Hedeoma* as a volatile oil, obtained by distillation from *Hedeoma pulegoides* Linné. The

\* Read at the meeting of the New Jersey Pharmaceutical Association, Newark, June 9.

sp. gr. was stated as 0.940 to 0.940, and the oil as soluble in two parts, by volume, of a mixture of alcohol 3 volumes, water 1 volume (approximately 70 per cent. alcohol by volume). "This is what is known in commerce as 'American Pennyroyal Oil.'" The later revision of the U. S. P. dismissed this title, and so we have now no official standard for *Oleum Hedeoma*.

A large portion of the Oil of Pennyroyal of commerce, however, is of European production, and is stated to be distilled from *Mentha pulegium* Linné. The European oil has a sp. gr. of 0.930-0.960, and is soluble in two parts of 70 per cent. alcohol. *Pulegone* is the most active constituent of both of the commercial varieties of Pennyroyal Oil, and is present in somewhat larger proportion in the European oil. It is a ketone  $C_{10}H_{16}O$ , in which the Carbonyl group, CO unites with two, alcohol radicals. Its boiling point is given by several authorities as from  $221^{\circ}C.$  to  $224^{\circ}C.$

The sample of oil under consideration was a limpid, pale yellow liquid having a distinct pennyroyal odor, with a mint-like tendency. The sp. gr. was 0.884, and it mixed clear in all proportions with 70 per cent. alcohol. The low specific gravity and the solubility at once indicated that the sample was not normal.

10 Cc. was fractionally distilled from a small distilling flask, 5 Cc. distilled over and was collected at a temperature below  $85^{\circ}C.$  This portion responded to the ethyl acetate test and other reactions for ethyl alcohol, proving that the sample was not pure Oil of Pennyroyal, but a mixture of which 50 per cent. was alcohol.

The fraction distilling between  $218^{\circ}C.$  and  $224^{\circ}C.$  was collected, as this should contain the *Pulegone*, the characteristic constituent of pennyroyal oil. It measured 1.6 Cc. corresponding to 16 per cent. in the sample, or, possibly, 32 per cent. in the original oil. It had the unmistakable odor of pennyroyal, greatly intensified and very persistent, and was soluble in 1.5 parts of 70 per cent. alcohol.

To prove that this was *Pulegone*, two identifying tests were adopted. *Pulegone* being a ketone, the iodoform test was applied as a group reaction, and the response was prompt with copious production of iodoform. *Pulegone* can be reduced by nascent hydrogen to form a menthol. A small portion was dissolved in dehydrated alcohol, metallic sodium added; after the reaction was completed the solution was diluted with water and extracted with petroleum ether. On evaporating the solvent the residue gave the distinct odor and taste of a menthol. The quantity worked with did not

permit of the making of melting point and optical rotation determinations.

From the above tests it was concluded that the sample was pennyroyal oil and mixed with alcohol to the extent of 50 per cent.

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## ARMY AND NAVY PHARMACISTS.

BY E. FULLERTON COOK, PH.M.

During the recent meeting of the American Pharmaceutical Association in Washington, the subject of Army and Navy pharmacists received much favorable attention. The Navy was represented by Lieutenant P. F. Dickens, who is assistant to Admiral Braisted, the Surgeon General, and was his personal appointment.

Dr. Ireland, Surgeon General of the Army, detailed Major A. P. Clark of his staff to tell the Association something of the plans which the Army are perfecting for commissioned pharmacists. The special committee on the Status of Pharmacists in the Government Service, consisting of Messrs. Cook, Beringer, Mayo, Eberle, and accompanied by the Secretary of the Council, Mr. Jos. W. England and by Mr. Leonard A. Seltzer, called on Surgeon General Ireland and Surgeon General Braisted, and discussed the entire situation. It was also possible for this committee to meet Admiral Washington, Chief of the Bureau of Navigation, and to have an interview with Secretary Daniels of the Navy.

Several days later, members of the Executive Committee of the N. A. R. D., including Mr. Samuel C. Henry, Charles H. Huhn and Theo. C. Hagenow, also called upon the Surgeon Generals, and General Ireland and Admiral Braisted carefully reviewed the situation. The feeling expressed by everyone who has learned of the latest developments is one of gratification and approval.

In the Army, the plan proposed by General Ireland for the establishment of a Medical Administrative Corps has passed both the Senate and the House, as a part of the Wadsworth Reorganization Army Bill and is now in conference in joint committee.

Since the above report was written, the Wadsworth bill has been finally passed by Congress and signed by the President of the United States. The Medical Administrative Corps, including the Division

of Commissioned Pharmacists, has become a reality. In the final draft of the bill, without the knowledge of the Surgeon General's office, the time required for service as a private before being eligible for a commission in the regular army, was changed from three years to two years. The highest rank in the Corps was reduced from major to captain. It is interesting to know that with the many criticisms of the Wadsworth Bill, this feature has never been questioned and as the General Staff of the Army have also given their approval of the establishment of this corps, it is reasonable to expect that when the Wadsworth Bill is finally passed, the Medical Administrative Corps will become a part of the law. Dr. Ireland has asked that pharmacists of military experience and of the highest technical training be selected for his assistance in the organization of the Pharmaceutical Section of this Corps. This officer, or possibly two officers, representing the several phases of pharmacy, would possibly be commissioned as a major in the Reserve Corps and then placed on active duty for the time necessary for organization.

Some additional details about the pharmacist's place in the new army will be of interest to every pharmacist. It will be in the reserve corps in peace time that pharmacy will have the greatest opportunity and the most attractive service. Here graduates of pharmacy who meet the other necessary requirements, including proper recommendation, and who have been approved by the proper officer in the Surgeon General's office, will be recommended for commissions as second lieutenants in the Reserve Corps, even though they have no military experience. It is understood that there will be about 1400 of these commissions available. The Medical Corps has secured for its training school, the old Indian school grounds at Carlisle, Pa., where training will be given in all sections of the corps, including the pharmaceutical division. Men who have been commissioned as second lieutenants, or with possibly a higher rating, due to experience in the World War, will be asked to take six weeks of training during the four years of enlistment. This training may be taken at one time or divided, and the school will be open throughout the year. As soon as an officer notifies the department that he is ready to take the training, he will be placed on active duty and his pay start before leaving home. The pay of a second lieutenant is about \$1700 per year.

In the Navy, the passage of the Darrow Bill is yet uncertain, but Secretary Daniels has agreed to assist in securing permanent

commissions for the 79 lieutenants of the Hospital Corps who were commissioned during the war, and Admiral Washington promised the committees that he would not oppose such action. Secretary Daniels recommended that the Darrow Bill or similar legislation be introduced in the next Congress, if it is not passed at this time.

## NEW ORGANIC ARSENIC COMPOUNDS.

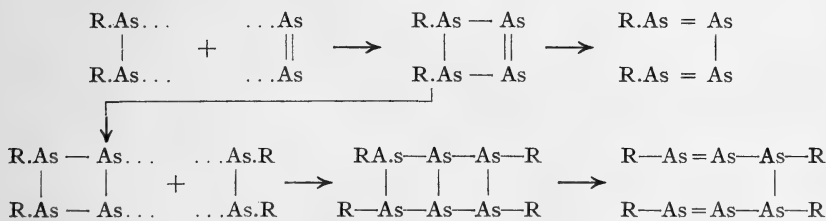
(Contribution from the Wellcome Chemical Research Laboratories.)

At the meeting of the Chemical Society on June 3rd a communication from the Wellcome Chemical Research Laboratories on "arsinic acids derived from guaiacol and veratrole" was read by Mr. R. G. Fargher.

The reaction between *p*-hydroxyphenylarsinic acid and potassium persulphate was shown to give 3,4-dihydroxyphenylarsinic acid, though in small yield and much contaminated with the unchanged acid. Separation of the two was difficult and their identity was most readily established by complete methylation and fractional crystallization of the product. 3-Amino-4-methoxyphenylarsinic acid, prepared from *p*-methoxyphenylarsinic acid by nitration and subsequent reduction, and 3-amino-4-hydroxyphenylarsinic acid were found to resemble *o*-aminoanisole and *o*-aminophenol in the difficulty which attended the decomposition of their diazo compounds, the energetic treatment necessary causing almost complete decomposition of the arsinic acids. The "Bucherer" reaction, by which the amino group in certain aromatic amines is converted into a sulphurous ester by the action of sodium hydrogen sulphite and subsequently replaced by hydroxyl by suitable means, was also unsuccessful.

The final method of attack—the Bart reaction, by which diazotized amines are coupled with sodium arsenite in alkaline solution with or without the presence of a catalyst such as copper powder—proved successful, and 3-methoxy-4-hydroxyphenylarsinic acid, 3-hydroxy-4-methoxyphenylarsinic acid and 3,4-dimethoxyphenylarsinic acid were prepared and their reactions studied, in particular the preparation of the corresponding nitroderivatives and the reduction of these. 3-Methoxy-4-hydroxy-5-nitrophenylarsinic acid underwent the normal arsenobenzene reduction with sodium hyposulphite, giving rise to 3,3<sup>1</sup>-dimethoxy-4,4<sup>1</sup>-dihydroxy-5,5<sup>1</sup>-

diaminoarsenobenzene, differing from "salvarsan" only by the presence of a methoxyl-group and resembling it closely in its properties and toxicity. 3-Hydroxy-4-methoxy-5-nitrophenylarsinic acid under similar conditions behaved abnormally, yielding a polyarsenide of the type  $R_2As_4$ ; while 3,4-dimethoxy-5-nitrophenylarsinic acid, which did not yield an insoluble reduction product, probably on account of sulphamic acid formation, on conversion into the amino acid and subsequent reduction with hyposulphite gave an abnormal compound of a second type  $R_2As_8$  or  $R_4As_6$ . The mechanism of the formation of these abnormal products and their possible formulation were discussed. It had been stated by Bertheim that a mixture of molecular proportions of two arsinic acids yielded solely the unsymmetrical arsenobenzene. More recently, Karrer had questioned the mechanism assumed by Bertheim and suggested that the symmetrical arsenobenzenes were first formed and then underwent "double decomposition." Utilizing the principle involved in the second suggestion, as this seemed to be in harmony with the observed facts, fission of the arsenic utilized to form the polyarsenides apparently succeeding rather than preceding reduction, formulae were evolved for the types  $R_2As_4$ , and  $R_4As_6$ , in accordance with the scheme:



The difficulty of completely proving homogeneity in these compounds was pointed out.

## BOTULISM DUE TO OLIVES.\*

The continued occurrence of fatal outbreaks of botulism poisoning caused by contaminated olives prompts our frequent reference to this situation. Many of the features of botulism outbreaks are still quite obscure; and in view of the urgent necessity for practical methods of prevention, every contribution to our knowledge of this form of food poisoning should be closely considered by sanitarians

\* From *Jour. Amer. Med. Assoc.*, May 1, 1920.

and health officials. The summary of the investigations of the Bureau of Chemistry on olive poisoning, given elsewhere in this issue,<sup>1</sup> contains material of general interest and practical application. Four of the five outbreaks reported in the summary were due to a toxin produced by the Type A of *Bacillus Botulinus*; the organism responsible for the fifth attack is not yet differentiated. Type A is the type found in California, and differs from the type present in the Eastern states and apparently from that observed in Europe. This summary leaves one in some uncertainty as to whether green olives as well as ripe olives have been implicated in botulinus poisoning. In the Montana outbreak, olives stuffed with pimento are considered to have been the source of the trouble, and in another instance "olive relish" in a tin container was the substance involved. It is not clear whether the "relish" was made of green or ripe olives, but it is certainly true that green and not ripe olives are commonly used for "stuffing." The title of the Bureau of Chemistry summary, on the other hand, seems to limit the poisoning to ripe olives, so that a clear statement on this point seems desirable. The important question as to whether or not *B. botulinus* contamination in canned food is always accompanied by physical signs of decomposition seems to be answered in the affirmative by the experience of the government investigators. They state that in all the material examined by them in which *B. botulinus* was present, the odor was distinctly offensive. This characteristic is a doubtful safeguard, however, since olives washed, iced or served with highly flavored foods may not betray their dangerous nature, particularly to persons unfamiliar with the natural taste of ripe olives. The source of the odor does not seem to be cleared up by these investigations. Whether the disagreeable smells are due to the products of *B. botulinus*, or whether the other microorganisms apparently always present in the imperfectly sterilized contents of the jar or can have given rise to the putrefactive conditions, is left undetermined by the evidence printed in the article cited. The conclusions of the Bureau of Chemistry worker that more efficient methods of sterilization should be employed, that brine packing should be modified, and that olives should be handled with the same degree of care and cleanliness as any other perishable food product seem abundantly justified.

<sup>1</sup> DeBord, G. G., Edmondson, R. B. and Thom, Charles: "Summary of Bureau of Chemistry Investigations of Poisoning Due to Ripe Olives," *Jour. Amer. Med. Assoc.*, May 1, p. 1220.



## THE TRUTH ABOUT VITAMINES.\*

By R. CECIL OWEN, B.Sc.

Most of us were brought up in the belief that the whole truth about food-stuffs was expressed by saying that the necessary and sufficient food factors were: proteins, fats, carbohydrates and inorganic salts; to which, of course, had to be added water. Till quite recently it was universally believed that given these factors, life could be sustained and growth promoted, and that in the absence of any of them a gradual starvation ensued. Careful and prolonged experiment, however, appears to make it certain that while the food factors referred to are necessary, they are not sufficient; that if animals are fed upon a mixture, in any proportion, of proteins, fats, carbohydrates, inorganic salts, and water, all in an absolutely pure condition, growth is first of all checked, then starvation supervenes and finally the animal dies. The seeming certainty of these things has led to the framing of the vitamine hypothesis. The results of certain experiments are explained by saying that the foods which are, in universal experience, found to be capable of sustaining healthy life, contain, in addition to the ordinary familiar factors, certain accessory factors; and to these has been given the generic name of "Vitamines." Let us illustrate our meaning by reference to some familiar substance. Chemically, butter and margarine may be—so far as one can say in the light of the chemistry of to-day—identical. It is therefore natural to suppose—the conclusion indeed seems irresistible—that in food value the two substances are identical. Yet what do we find? If rats are fed for a time on a diet containing butter the diet being sufficient for normal life, and if the diet be after a time changed so far as to substitute certain margarines, or lard, for the butter, it is found that the animals experimented upon cease to grow (if young enough to grow), and decline and die. Upon such lines a large number of experiments, very carefully made, have been carried out. The general conclusion arrived at is this, that the substitution of artificially prepared (*i. e.*, absolutely pure) fat—or even lard, for the fat contained in a diet sufficient to sustain life, led to the rapid decline and early death of the animal; and the theory deduced by way of explanation is that certain fats contain "vitamines" while others do not.

\* From *The Prescriber*, May, 1920.

It is extremely necessary to bear in mind what part of our subject is indisputable fact, and what part theory, hypothesis, or guessing; otherwise no adequate grasp of the vitamine theory is possible. In an actual experiment—there is space only for the mention of one—rats were fed upon a mixture of caseinogen, starch, cane-sugar, lard, and inorganic salts, all very carefully purified: resulted in decline and death. Rats were then fed for a limited period on this “pure” diet; decline again set rapidly in. Then a small allowance of milk was added each day, with the result that a perfect food was produced, and the animals once again flourished.

Enough has now been said to illustrate the lines upon which experiments have been made. Let us now outline the conclusions arrived at. Certain fats, as we have seen, contain “vitamines,” and such fats are necessary food factors. These vitamines are known as “A” vitamines, or “fat-soluble” vitamines. But there are others. There is “B” vitamine, or “water-soluble” vitamine, contained markedly in yeast-extract, for example. And there is a third, known (somewhat clumsily) as “anti-scorbutic” vitamine, and found nowhere so abundantly as in fresh lemon juice. In the light, then, of our present knowledge, we may say that the whole truth about food-stuffs is contained in the following statement: Foods necessary and sufficient to sustain animal life contain, in addition to proteins, carbohydrates, fats, inorganic salts and water, three “vitamines” known as A (fat-soluble), B (water-soluble), and C (anti-scorbutic).

Now let us, with all possible brevity, give some account of the vitamine content of the foods in common use—not, of course, exhaustively, but only for the sake of intelligibility.<sup>1</sup> V. A. is found in butter, cod-liver oil, suet, fish oil, nut butters (which *nota bene*), lean meat, liver, kidney, sweet breads, fish only if fat, whole milk dried or raw, cheese, eggs, wheat germ, linseed, haricot beans, cabbage, lettuce, spinach, carrots, raw potatoes, bananas, nuts; but not in vegetable margarines (N. B.), lard, olive oil, cacao butter, linseed oil, hardened fats, white fish, skim milk, polished rice, or meat extracts.

V. B. is found in lean meat, liver, kidney, heart, milk (whole, skim, raw, or dried), eggs, wheat, peas, cabbage, lettuce, spinach, carrots, bananas, nuts, yeast extract, dried yeast; but not in butter,

<sup>1</sup> In what follows V. A. stands for fat-soluble vitamine, V. B. for water-soluble and V. C. for anti-scorbutic.

cream, olive oil, white flour, custard powders, pea flour, or meat extracts.

V. C. is contained in lean meat, liver, raw milk, whether whole or skim, germinated pulses, cabbage fresh or cooked, fresh juice of the Swede, carrots, cooked potatoes, fresh beans, lemon juice fresh or preserved, lime juice only if fresh, orange juice, raspberries, apples, tomatoes; *but not in preserved lime juice* (N. B.) nor in yeast, meat extracts, tinned meats, eggs, wheat, white flour, custard powders, dried peas, nor in any oils animal or vegetable.

The only food, apparently, rich in all three vitamines is the humble cabbage (fresh); while white wheaten flour, pure corn-flour, and polished rice contain no vitamines whatsoever, and the same thing is true, alas, of beer.

It has long been known that the cause of scurvy was the lack of fresh vegetables and fruit, and to a smaller extent of fresh meat. To-day we say, with an effort of greater precision, that scurvy owes its incidence to want of vitamine C, the anti-scorbutic vitamine. Attempts have been made to investigate this question quantitatively as well as qualitatively. Thus it has been shown that by removing green stuff from the diet of guinea-pigs and feeding them on grain and water only, scurvy, with its characteristic features of hemorrhage and bone-changes, was induced, and from it the animals died in from twenty to forty days. Similarly scurvy was prevented, or cured, by the addition to the grain and water diet of fresh cabbage, carrot, cranberries, sorrel, or dandelion leaves. Then the anti-scorbutic potency of various food-stuffs was ascertained—only roughly, of course—by determining the minimum quantities which had to be added to the grain and water diet so as just to prevent scurvy. In this way it has been found that for guinea-pigs—and, it is inferred, for the human subject also anti-scorbutic food-stuffs, may be classified as follows in *descending* order of value:

1. Raw cabbage, fresh lemon juice, fresh orange juice (greatest value).
2. Runner beans, juice of Swedes.
3. Germinated lentils, cooked cabbage, preserved lemon juice, fresh lime juice.
4. Carrot juice, beetroot juice, onion, cooked potato.
5. Grapes, apples, tamarind, mango, kokum, meat juice, raw milk (smallest positive value).
6. Grain (whole), gum, bran, polished rice, whole dry pulses,

desiccated vegetables, pickled vegetables, preserved lime juice (N. B.), eggs, tinned meat, yeast (of no—V. C.—value).

I quote the following from the N. H. I. Medical Research Committee's "Report on the Present State of Knowledge Concerning 'Vitamines:' "

"The anti-scorbutic accessory factor is found in nature associated with living tissues in which metabolic processes are still proceeding. When these active processes cease or are greatly reduced, as in seeds, or when the tissues are destroyed, as in heating or drying, the anti-scurvy 'vitamine' also disappears. In the case of seeds it is created anew during germination."

It is not then to be wondered at that cooking is distinctly destructive of the vitamine in anti-scorbutic food-stuffs. Experiments made with cabbage leaves point to the following conclusions: When heated in water for one hour at temperatures ranging between 80° and 100° C., 90 per cent. of the vitamine is destroyed; when heated for one hour at 60° C., or for twenty minutes at 90–100° C., the loss of vitamine is found to be 80 per cent. An interesting practical conclusion is this, that it is better to cook anti-scorbutic foods quickly at a high temperature than slowly at a lower temperature. The vitamines are more quickly destroyed in an acid or alkaline medium. Vegetables should, therefore, be boiled in pure water, without the addition, *e. g.*, of soda.

There are now good reasons for believing that beri-beri is a deficiency disease; and that, moreover, its incidence is due to a lack of "vitamine B," which is therefore known as "anti-neuritic" vitamine. As long ago as 1897, Eijkman, a medical officer to a prison in Java, had a number of beri-beri cases in his charge. He observed that his poultry, fed largely on rice refuse, sickened and died of a disease whose symptoms resembled those of the beri-beri of his patients. There was paralysis and there was a marked degeneration of the peripheral nerves. These observations were the starting point of a series of experiments which compelled the conclusion that avian polyneuritis was the counterpart of human beri-beri. Experiments conducted on lines already briefly described warrant the belief that beri-beri is caused by the absence, and can be cured by the restoration, of vitamine B to an otherwise unexceptionable diet. Polished rice has undoubtedly been the main offender in causing beri-beri; and it has been abundantly proved that if to polished rice be added the constituents (embryo and pericarp) re-

moved during milling, the diet so formed is capable of preventing the disease. The following list of food-stuffs is arranged in order of merit so far as their anti-beri-beri value is concerned: Rice germ, wheat germ, lentils, yeast (pressed), egg yolk and ox liver (equal), peas (dried), wheat bran, beef muscle, potatoes.

With reference to the effects of heat upon vitamine B it may be said that, broadly speaking, heat has no marked detrimental action, till temperatures of over  $100^{\circ}$  C. are reached. Even prolonged exposure to temperatures of less than  $100^{\circ}$  C. has little or no effect, but when this temperature is exceeded, especially if by more than  $20^{\circ}$ , rapid deterioration is observed. It follows, then, that bread, biscuits, etc., should be baked at a temperature not exceeding  $100^{\circ}$  C.; as also that *tinned foods of all descriptions*, exposed as they are for various reasons to high temperatures, *are almost wholly lacking in vitamines*.

Now let us return to vitamine A. We may say that there is irresistible evidence—of a similar kind to that already briefly recounted in connection with vitamines B and C—to precipitate the conclusion that vitamine A is the “cure” for rickets and other wasting diseases, and is conveniently described as “anti-rachitic” vitamine. Experiments made upon puppies show that diets I and II prevented rickets, while diets III and IV did not.

Diet I.—Whole milk, porridge, rice, NaCl.

Diet II.—Whole milk, white bread, NaCl.

Diet III.—Separated milk, white bread, linseed oil, yeast, NaCl.

Diet IV.—Separated milk, white bread, linseed oil, yeast, orange juice, NaCl.

Experiments made in great numbers confirm the conclusion that rickets is caused by the absence from an otherwise perfect diet of certain fats and other substances (*vide supra*), and may be cured by a restoration to the diet of these food-stuffs. The theoretical conclusion is that ricket-preventing food-stuffs contain a hypothetical substance called “Vitamine A,” or “anti-rachitic vitamine,” supposed also to be fat soluble.

The effect of heat upon anti-rachitic substances is important. They are the most stable of all the vitamine foods in the presence of heat. Thus butter is de-vitaminized by exposure to a temperature of  $100^{\circ}$  only after four hours. The “hardening” of oils by the action of nascent hydrogen is a swift and certain means of destroying their vitamines.

We have seen that the absence from a diet of any one of the three vitamines gives rise to a corresponding disorder: The absence of vitamine A causes rickets, of B beri-beri, and of C scurvy. Now, there is good evidence for believing that another disease, pellagra, which is endemic in Northern Italy, Roumania, and in certain parts of North America, is due to the absence of four food factors—two of them vitamines—though whether all four “absences” have to be present together or only in pairs is a point not yet solved. The four pellagra-producing factors are these: (1) Shortage of vitamine A; (2) shortage of vitamine B; (3) shortage of inorganic salts; (4) shortage of proteins. It is at any rate certain that no one factor alone can produce pellagra, but that at least two of them together must be present. The symptoms of pellagra are gastrointestinal disturbances and bilateral symmetrical dermatitis. But the whole subject of the relation of vitamines to disease is in its infancy. The question of pellagra, by offering a combination of causes, opens up a complicated field for research.

The most astonishing thing about vitamines is that they are apparently non-existent. We are often told, somewhat loftily, that “vitamines have not, as yet, been isolated.” This is only a part of the truth. The whole truth is *that their existence has not yet been demonstrated*. If this declaration, coming at the end of an article on vitamines, sounds paradoxical, I must add a word or two in explanation. We have seen that butter differs from vegetable margarine in certain important particulars. Butter has properties which margarine has not. But this fact, indisputable as it is, is a long way from warranting the conclusion that butter = margarine + vitamine. Tartaric acid has a property (“optical activity” is it called) which racemic acid has not, and both acids are chemically identical. But this fact does not warrant us in saying that tartaric acid contains “optamine,” while racemic acid does not. The truth is that tartaric and racemic acids are isomeric, and are identical in every way except as to the arrangement of their atoms within the molecule. A similar hypothesis seems preferable to explain the important differences between the glyceryl oleate, etc., which we call butter, and the same chemical compounds which we call margarine. It is an indispensable rule, in framing hypothesis to explain phenomena, not to go beyond what is warranted by data. The Law of Parsimony applies here. That hypothesis should be chosen which follows the most closely on the heels of the facts, which puts

the smallest strain on one's credulity, and which is simplest and lies nearest at hand. It is simpler and less erratic, and altogether more convincing, *in view of all the facts*, to postulate isomerism as the explanation of the differences between certain natural and artificial food-stuffs, rather than to guess at the existence of new substances which nobody has yet isolated, or even detected, and about which nobody knows anything whatever. For nobody, observe, knows anything about vitamins, but only about butter, lean meat, fruits, yeast, and so forth. Hence it is likely that the most fruitful hypothesis will prove to be that of biological isomerism rather than that of "vitamins."

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## ALCOHOL: ITS RELATION TO SCIENCE AND INDUSTRY.\*

BY WILLIAM L. CROUNSE.

In this presence it would be a waste of words to undertake to emphasize the importance of alcohol in pharmacy. I feel, however, that in view of the extraordinary events of the past year and the conflict of counsels as to the policy the drug trade should pursue in protecting itself against the hazards incident to the enforcement of the unprecedented provisions of the Volstead Act, I am justified in appealing to you to do your bit in securing for alcohol the official recognition to which it is entitled as the most essential chemical raw material known to industrial science.

The man in the street is apt to consider distilled spirits solely as the means of producing a condition of more or less delightful exhilaration, with a dark brown taste the morning after. To the extreme prohibition enthusiast all forms of spirits are anathematized as the Demon Rum. But few persons outside the circle of those who actually employ alcohol in science and industry appreciate its indispensable character, or realize that if its supply were cut off thousands of manufacturing plants would cease operations, hundreds of thousands of men and women would be thrown out of employment and the science of medicine relegated to the dark ages.

While, therefore, the law of the land, which we all cheerfully obey, requires that adequate safeguards shall be thrown around the use of alcohol to prevent its diversion to beverage purposes,

\* Address delivered at the meeting of the American Pharmaceutical Association, Washington, May, 1920.

yet we who realize its value to science and the industrial arts should not hesitate to demand that it shall be available for every legitimate purpose and on terms that represent a minimum of expense and hardship to the user.

#### USE OF DENATURED ALCOHOL.

No development in the utilization of alcohol is more significant of its great importance to industry than the enormous increase in the consumption of denatured spirits since the passage of the so-called free alcohol law of 1906. It was my pleasant task to assist the manufacturers of the country in the efforts to secure the passage of that statute and it has been a matter of great satisfaction to me to note the rapid development of the use of denatured spirits under its beneficent provisions. Beginning in 1907 with a total consumption of completely and specially denatured alcohol of 1,780,276 wine gallons, the total rose in 1914 to 10,404,975 gallons. In 1914 the World War began and the demand for alcohol, first, for the manufacture of smokeless powder, and, second, for the production of our allies and for the United States of various gases, including the deadly mustard gas, received an enormous impetus, consumption rising rapidly until in 1917 the peak was reached with a total of 55,679,597 gallons, of which 10,508,919 gallons were completely denatured and 45,170,678 gallons specially denatured.<sup>1</sup>

Fiscal Years.	Completely Denatured. Wine Gallons.	Specially Denatured. Wine Gallons.	Total. Wine Gallons.
1907.....	1,397,861.16	382,415.19	1,780,276.35
1908.....	1,812,122.38	1,509,329.35	3,321,451.73
1909.....	2,370,839.70	2,185,579.15	4,556,418.85
1910.....	3,076,924.55	3,002,102.55	6,079,027.10
1911.....	3,374,019.92	3,507,109.94	6,881,129.86
1912.....	4,161,268.56	3,933,246.44	8,094,515.00
1913.....	5,223,240.78	4,608,417.76	9,831,658.54
1914.....	5,213,129.56	5,191,846.03	10,404,975.59
1915.....	5,386,646.96	8,599,821.81	13,946,468.77
1916.....	7,871,952.82	38,807,153.56	46,679,106.38
1917.....	10,508,919.34	45,170,678.29	55,679,597.63
1918.....	10,328,454.61	39,834,561.48	50,163,016.09

Notwithstanding the rapid increase in the consumption of denatured alcohol in this country, at the time of the beginning of the

<sup>1</sup> The following table shows the production of alcohol both completely and specially denatured by fiscal years, since the passage of the free alcohol law of 1906:



great war, Germany was producing ten gallons to our one, a fact which has had an important bearing upon German supremacy in the vast field of industrial chemistry.

The part borne by alcohol in the war is worthy of much more space than the limits of this brief paper afford. It is interesting however, to recall the fact that when the great German offensive was on in 1918 and the British and French armies stood "with their backs against the wall," General Pershing sent an order to the United States for 1,000 tons of mustard gas per day, to be delivered forthwith. To produce a ton of mustard gas requires a ton of alcohol; hence to arrange for the filling of this enormous order, the War Industries Board was obliged to mobilize the entire distilling industry of the United States and turn it for the time being from all other classes of production to the making of alcohol. But for the intervention of the armistice it is probable that the distillers of the United States for many months would have been able to furnish nothing but the raw material for the deadly gas that was so signally aiding the Allies in the winning of the war.

You are all familiar with completely denatured alcohol, which, since 1906 has been permitted to be freely sold and used for a variety of industrial and domestic purposes. Few of you, however, have been brought into close contact with specially denatured alcohol which, after distillation, is modified by the use of a large number of different chemical agents for consumption in an enormous variety of industries. A single formula of the thirty-five now in use has been approved for employment in the manufacture of nearly two hundred articles ranging from smokeless powder to artificial flowers, and from transparent soaps to the ink used in the interstate branding of meats.

#### ALCOHOL IN MEDICINE.

It is not surprising that the average layman should be at a loss to know where to turn for reliable information concerning the function of alcohol in medicine. This uncertainty is largely due to wholesale misrepresentation, in part deliberate and in part due to ignorance, by over-zealous partisans of the cause of prohibition. It has been one of my most exasperating experiences during the past two or three years to listen to statements made before important committees of Congress by certain of these zealots to the effect that, if the supply of alcohol should be immediately cut off, medical science would in

no way be embarrassed, the preparation and administration of drugs would in no respect be restricted or inconvenienced, while the science of therapeutics would actually be benefitted thereby.

It is usual for these enthusiasts, none of whom claim any knowledge of medicine, pharmacy or chemistry, to take as a text a statement of some physician or a resolution adopted by some medical society to the effect that the position of alcohol as a therapeutic agent is more or less doubtful, and urging that physicians use a greater degree of restraint in prescribing alcoholic stimulants.

Upon these premises—which, of course, are debatable ground—is based an argument that alcohol is no longer necessary in medicine, and I have heard some of the more extreme advocates of this theory declare that no exemptions should be provided in the Federal Prohibition Act for standard drugs, proprietaries, toilet articles or flavoring extracts.

Of course, what the physicians who are quoted in this connection have said—and there is a wide divergence of expert opinion on the subject—has been confined exclusively to the use of spirits for their direct therapeutic or stimulating effect, and has had no bearing whatever upon the employment of alcohol as an extractive agent, solvent or preservative.

I think it is only fair to say that in the majority of cases these zealous gentlemen have been entirely ignorant of the technical reasons for the employment of alcohol in the manufacture of medicines, and have been honest in their belief that such spirits as are used in the average alcoholic medicinal preparation are deliberately introduced for the purpose of stimulating the patient, the physiological effect of the spirits being counted upon by the manufacturer or prescriber in exactly the same way that the other ingredients are relied upon to produce certain results.

Conceding, however, that these gross misrepresentations have been made in good faith, what shall be said of the arguments predicated upon such ignorance, or of law-makers or administrators who permit themselves to be swayed by such influences?

While the efforts which pharmacists and chemists in many lines of industry have been making in recent years to discover satisfactory substitutes for alcohol, especially for purposes of solution and preservation, are in line with the broad basic principles underlying the progress of science, nevertheless they should not mislead us into assuming a timid or equivocal attitude with respect to alcohol, or

deter us from defending our right to use it whenever and wherever the rules of pharmacy and chemistry require. The mere fact that there are abuses in the use of alcohol, which nature, for some inscrutable reason has made intoxicating, should no more deter the reputable manufacturer or physician from employing it in the preparation of drugs than occasional murders or suicides by the use of poisons should operate to eliminate all poisonous drugs from the Pharmacopoeia.

There are some sound reasons why scientific research should be directed toward the discovery of substitutes for alcohol. High cost is one of them. This consideration alone is steadily operating to reduce the amount of spirits employed in every preparation in which it is feasible to make any reduction whatever. Never before in the history of the drug trade has it been so difficult to obtain a supply of alcohol, and the mounting price and difficulty of procurement have constituted incentives that would have stimulated experimentation in a much greater degree if the prospect for the discovery of satisfactory substitutes had been more encouraging.

Every retail druggist will welcome the efforts made by the Pharmacopoeial Committee to reduce the alcoholic content of official preparations. Any substantial reduction attained will tend to curtail the cost of production and to render official preparations less liable to be diverted by degenerates to beverage purposes, but the standards finally fixed by the United States Pharmacopoeia and National Formulary should be promptly accepted as irreducible minima, and pharmacists the country over should unite in demanding the right not only to employ alcohol in accordance with these standards, but also to obtain an adequate supply with the least possible difficulty and expense.

#### HOUSE-CLEANING OF DRUG TRADE.

The retail drug trade may well congratulate itself upon the splendid job of house-cleaning it has done in casting out fake alcoholic proprietary medicines, in putting out of business whiskey sellers thinly disguised as druggists, and, more recently, in confining the sale of wines and liquors to strictly legitimate purposes. In this movement the retailers are now enjoying the hearty coöperation of the drug jobbers who appreciate that if the trade is to be kept clean-handed the wholesalers must support the highest standard adopted by the retailers and refuse to sell alcoholic preparations to anyone

under circumstances which would justify the suspicion that they are to be diverted to beverage purposes.

In liberalizing the original House draft of the Volstead Act for the purpose of providing adequate exemptions for the drug and allied trades, the proviso that exempted articles must be "non-potable and incapable of being used for beverage purposes," was stricken out, and the phrase "unfit for beverage purposes" was substituted. In view of this concession, the Congressional leaders, at the instance of the representatives of the drug trade, inserted as a corollary an additional provision, in part as follows:

"Any person who shall knowingly sell any of the articles mentioned in paragraphs *a*, *b*, *c* and *d* of this section for beverage purposes, or any extract or syrup for intoxicating beverage purposes, or who shall sell any of the same under circumstances from which the seller might reasonably deduce the intention of the purchaser to use them for such purposes, or shall sell any beverage containing one-half of one per centum or more of alcohol by volume in which any extract, syrup or other articles is used as an ingredient, shall be subject to the penalties provided in Section 29 of this Title."

While this provision makes it incumbent upon every house in the trade, whether manufacturer, jobber or retailer, to use the utmost care to prevent the diversion of alcoholic preparations to beverage uses, in my opinion it imposes a special obligation upon the jobber, for it is in his power to control the distribution of alcoholic medicinal preparations, toilet articles, etc., to a marked degree. As illustrating my own view of the jobbers' duty in the premises—a view which I am confident has been quite generally accepted throughout the wholesale drug trade—I will quote the following extract from an address which I made before the National Wholesale Druggists' Association at its convention held in New Orleans last November:

"Under the provisions of the Volstead Act it becomes the duty of every manufacturer or distributor of an alcoholic preparation which might be diverted to beverage purposes to carefully scan every order for such goods he may receive and to refuse to sell such articles in quantities in excess of what he believes to be the reasonable requirements of the purchaser for strictly legitimate purposes. It is, of course, impossible to lay down any hard-and-fast rule with respect to the quantities of various articles which may properly be sold. No two purchasers necessarily have exactly the same requirements, but it is believed that every jobber is in position to

know if an order for any of the articles in question is in excess of the actual needs of the buyer for legitimate purposes. In no case should an order be filled for the maximum quantity called for if the jobber is in doubt as to the purpose for which the goods will be used.

"For their own protection, members of the National Wholesale Druggists' Association should make and preserve such records as will clearly show their intention to observe the spirit as well as the letter of the law, and their daily practice pursuant thereto. No intricate system need be adopted, but it is suggested that such records should be kept as will enable jobbers to compare incoming orders for the alcoholic preparations in question with those previously received from the same customers to determine whether by increasing quantities, or purchasing more frequently, such customers are accumulating unnecessarily large stocks. A record should certainly be made of all orders the quantities of which jobbers find it necessary to reduce, as such data constitute the best possible evidence of an intention to cooperate with the Government in the strict enforcement of the law. It will also be well to preserve in the same file, copies of correspondence relating to reductions of orders, together with copies of all circulars or other memoranda that may be sent out to the trade; also copies of instructions to salesmen, office employees, etc., etc.

"It should be borne in mind that the fact that an article is made in accordance with the United States Pharmacopoeia, or the National Formulary does not take it out of the category of alcoholic preparations which may be improperly diverted to beverage purposes. Nor does the high alcoholic content of a preparation necessarily include it within the suspected category, for it is conceivable that a preparation might be nearly all alcohol and yet contain a small quantity of a drug so powerful as to render it impossible to drink it. The test is whether the goods are likely to be used as substitutes for intoxicating beverages; if so, everything possible should be done to prevent their sale in quantities exceeding the demand for the legitimate purposes for which they are intended."

#### REGULATIONS UNDER VOLSTEAD ACT.

The entire drug trade, and in fact all users of alcohol who are thereby subject to official supervision, are to be heartily congratulated upon the present personnel of the Prohibition Unit of the

Internal Revenue Bureau. Mr. Kramer, the Prohibition Commissioner, is discharging his duties with an intelligence, an impartiality and a resourcefulness that have already inspired the confidence of every one who has had dealings with him. In Deputy Commissioner Gaylord, we have one of the most experienced, far-sighted and progressive men in the entire Government service. Mr. Gaylord is an expert not only in Internal Revenue Law and regulations and in the administration of statutes requiring tact as well as skill, but he is probably the best-informed man in the Internal Revenue Bureau with regard to the industrial position of alcohol. His technical knowledge and his keen appreciation of the necessity for administering the Prohibition Law in such a way as to minimize the restrictions and annoyances imposed upon manufacturers who are obliged to use alcohol, render him not only an exceedingly useful aid to Commissioner Kramer, but an official who can be counted upon at all times to give the fullest possible consideration to legitimate interests while executing this difficult statute in accordance with its spirit as well as its letter.

That there is much room for improvement in the present code of regulations the officials of the Prohibition Unit will be the first to concede. The present code of rules was framed to cover uncharted ground. There were no precedents for supervision of the character and extent required by the Volstead Act, and much that has been done will doubtless be undone; nevertheless, the regulations as a whole have thus far disclosed as few faults as have been developed in the case of any similar code which the Government has heretofore adopted under any other statute, and it has already been demonstrated that the officials feel no pride of authorship, but stand ready to modify any regulation when it can be shown that it can be improved in any important respect without sacrificing the validity of the statute.

The present method of obtaining alcohol upon permits, known as Form 1410, leaves much to be desired. It is clumsy and costly and its use frequently involves indefinite delay. It does not adequately protect the Government, but discriminates in favor of unprincipled persons seeking to exploit the statute and against the honest, conscientious manufacturer or dealer.

I recently had the honor to be chairman of a committee representing the drug and allied trades, which after extended conferences with representatives of all branches of our industries recommended

to the Bureau the abandonment of Form 1410 as applied to all purchases of original stamped packages of alcohol, and the substitution therefor of a "floating" permit similar to that used successfully for many years in the procurement of specially denatured alcohol. Such a permit would bear upon its face a statement of the maximum quantity of alcohol which the holder would be allowed to purchase during a ninety-day period under his outstanding bond and could be lodged with any distiller and drawn against from time to time, by mail, telegraph or telephone, until the limit of the bond should be exhausted. The distiller or dealer making shipment on this floating permit would enter the amount thereon and at once mail a notice of the shipment to the Prohibition Director of the district and to the Prohibition Commissioner in Washington.

Under existing conditions, and especially because of the scarcity of alcohol, it is difficult to procure spirits promptly and in the great majority of cases orders on Form 1410 have to be returned to the holder of the permit for the purpose of reducing the quantity ordered. Thus vexatious delays occur and holders of permits to use alcohol for manufacturing purposes frequently find themselves without any of this very necessary material at hand. The existing requirement that all the copies of Form 1410, of which a large number are required each month, shall be sworn to, is, of course, a wholly unnecessary expense, for if a manufacturer holds a permit no further evidence of his right to use alcohol should be required.

The importance of the reform that would be effected by the substitution of a single floating permit for the numerous copies of Form 1410, is suggested by the fact that at the time of the recent conference of our trade committee with the officials of the Prohibition Unit, one Prohibition Director was being called upon daily to sign 12,000 individual permits to purchase. Relieved of this purely clerical work, the entire supervisory service could be devoted to the investigation of applications for permits, a task of crying necessity in view of the large number of permits perfunctorily issued during the days immediately following the taking effect of the Volstead Act. Many unscrupulous persons, seeking to reap a harvest in a short time through the diversion of alcohol and other intoxicating liquors to beverage purposes, procured permits which they could not have obtained upon full investigation, manufactured quantities of fake medicine or toilet articles or spurious liquors, and after marketing them at enormous profits decamped for parts un-

known, leaving nothing behind them but a smirch upon the good name of legitimate industries and an acute heartache in the Prohibition Unit. I am glad to say that these cases are being most carefully investigated and large numbers of permits will undoubtedly be cancelled.

There are many incongruities in the law and regulations that I am confident will be corrected in a short time. For example, what would be more ridiculous than a rule which permits the house physician of a hotel to prescribe a pint of whiskey for a transient guest staying perhaps but a night in a place, but which renders the guest a criminal, liable to serve a term in the penitentiary, if he attempts to take the whiskey with him when leaving the hotel, thus making it necessary for him to consume the entire pint at a sitting to keep out of jail. I am glad to be able to say that the Bureau is now considering the feasibility of authorizing a special label to be attached to containers of spirits regularly prescribed by physicians, showing the name and permanent address of the patient, the name and address of the physician and of the druggist from whom the spirits were purchased and any additional data that may be deemed advisable. Of course, it hardly need be said that it would be next to impossible to convict of a crime a person who, having regularly received a pint of spirits upon a physician's prescription, should be detected in the attempt to convey same from the hotel where he chanced to be stopping to his permanent home; nevertheless, it is important that such a matter should be provided for by regulation and not left to the variable judgments of special agents, district attorneys and courts in a hundred different jurisdictions.

Retail druggists of late have been rendered apprehensive by persistent reports, current for some time, that the Prohibition Commissioner is preparing to issue an order limiting to 100 gallons the amount of alcohol in all forms they will be permitted to procure in any 90-day period. These reports are erroneous though they have a basis in the fact that the Commissioner has been giving considerable attention to the problem of the practicability of determining the maximum quantity of spirits which a retailer can legitimately use in the course of three months.

Up to the time this was written, no hard-and-fast rule had been adopted and there appear to be sound reasons why it is impracticable, if not impossible, to fix a limit that would not work great hardship if it were made at all restrictive. For example, an amount



of alcohol which would be ample for a small druggist with a limited prescription business who is in the habit of purchasing rather than making the bulk of his alcoholic preparations, would be wholly inadequate to meet the needs of another druggist with an equal volume of business who stood well with the doctors because of his careful methods and who, like the old school pharmacist, makes his own tinctures, two or three successful little proprietaries of his own and other articles which are now commonly purchased of the wholesaler.

I feel confident that the Prohibition Commissioner will take a reasonable view of this whole matter and that if any limit, other than the size of the druggists' bond, is adopted, it will be sufficiently elastic to avoid all hardship.

Manufacturers, jobbers and retailers, alike, have been put to a great deal of trouble and considerable expense by the Bureau's ruling requiring monthly reports concerning all alcohol consumed. In view of the fact that the only parties allowed to employ non-beverage alcohol for manufacturing purposes or for sale are presumed to have been carefully investigated by the Bureau, and of the further fact that unscrupulous persons would have no difficulty in falsifying these reports in such a manner as to escape detection, it is natural that the casual observer should jump to the conclusion that the time and the money they cost the trade are out of all proportion to their practical value to the Bureau.

I think we should suspend judgment on this matter, for a while at least, and give the report system a fair trial. It is possible that it may prove of sufficient value to the Bureau to justify its permanent retention. If so, it may be practicable to simplify the reports somewhat and perhaps to require them to be rendered quarterly instead of monthly, which, in many cases, would substantially reduce the labor of the permit holder.

I know that our friends in the Internal Revenue Bureau would give even greater consideration to the question of demanding additional reports or of requiring additional records to be kept if they could see the cold figures representing their cost to the business men of the country. I have in my possession letters from three large manufacturing and jobbing houses in the drug trade in which the extra cost of the narcotic and alcohol regulations is put down in one case as exceeding \$10,000 per annum, and in another as more than \$12,000, while in the third case it is estimated that the cost exceeds 10 per cent. of the value of the entire output of all classes of com-

modities. While the extra cost to the average retailer is not very much as measured in dollars and cents yet, multiplied by the many thousand dealers now doing business in the United States, the aggregate must run far into the millions.

In this connection I would bespeak your patient consideration for any personal eccentricities that may be developed by Mr. Kramer's staff of Prohibition Directors. You who are accustomed to deal with the veteran experts of the Internal Revenue Service may frequently be tempted to become a bit testy over the super-zeal or lack of knowledge on the part of some of these new officials. I am confident, however, that none of you have had as comprehensive an experience in dealing with these gentlemen as has fallen to my lot since the 16th of January, and I take pleasure in testifying to their general intelligence, their impartiality and their uniformly good intentions. Mr. Kramer is following their movements with a keen eye and will not hesitate to put them on the right track whenever they go wrong. I am certain, however, that within a reasonable length of time you will find them discharging their duties with tact and discretion, as well as with properly directed zeal. There will necessarily be a few exceptions to this rule, but whenever you encounter one you have only to remember that Mr. Kramer's permanent address, 365 days in the year, is 1330 F Street, Washington, D. C.

#### PHARMACISTS' ATTITUDE TOWARD ALCOHOL.

Action taken during the past year by organized retailers, and many informal statements made by individual druggists indicate that the retail drug trade is now divided into three separate camps with respect to a definite attitude toward the question of selling or handling any form of intoxicating liquors.

The members of one contingent have decided that it is the function of the retail drug trade to provide anything that a reputable physician may order on prescription, and, therefore, they do not hesitate to carry and sell whiskey and other intoxicating liquors to be dispensed solely on prescriptions. They also carry non-beverage alcohol which they use for prescriptions and general manufacturing purposes and sell in medicated form in small quantities in accordance with the regulations.

The second class, while handling and selling non-beverage alcohol, have decided that they will not dispense whiskey or other intoxicating liquors even on the prescription of a physician. They sincerely

believe that doctors as a class are in the habit of prescribing too much whiskey and other intoxicating liquors, and would use less if it were more difficult to obtain.

The third class have determined to handle and to sell neither whiskey nor other intoxicating liquors, including even non-beverage alcohol, for any purpose whatever. According to certain members of this class they not only desire to be rid of the inconvenience incident to the supervision of dealers in intoxicating liquors, but they believe that refusal to sell them, even on a prescription of a physician, or to handle alcohol in any form, for any purpose, will be approved by the general public and especially by the officials of the Government charged with the supervision of this traffic; also that the refusal to handle intoxicants of any kind will aid materially in advancing the ethical position of the retail drug trade and go far toward correcting false impressions that have found lodgment in the public mind as the result of the acts of a few unscrupulous members of the trade.

Without attempting an analysis of the attitude of these three sections of the trade, it may be well to call attention to certain important considerations. It is an incontrovertible fact that a large and eminently respectable contingent of practicing physicians believe that intoxicating liquors are of decided value in the treatment of certain diseases and physiological conditions. Their right to prescribe them is specifically conceded by the provisions of the Volstead Act, which thereby imposes upon the Internal Revenue Bureau the exceedingly difficult task of policing their production, distribution and administration.

It would be an ideal condition, in view of the fact that more or less intoxicating liquor is certain to be sold on physicians' prescriptions pursuant to the Volstead Act, if some quasi-official dispensing system could be adopted, possibly under the supervision of the Public Health Service, but the Government appears to be taking no steps looking to the organization of any such system and it seems to me that the retail drug trade might well take this matter up vigorously and pursue it with the greatest possible energy until some adequate system has been devised. Physicians are contending with considerable emphasis that the retail druggists owe it to the medical profession, to which they are the recognized purveyors, and to the public which they must be ever ready to serve, that they shall do more than merely determine that they will not sell intoxi-

cating liquors on physicians' prescriptions; they should use the great influence, which collectively they wield, to aid in working out a solution of this problem in a thoroughly practicable manner.

Under existing conditions, and in default of a semi-official dispensing system, an anomalous situation prevails. The Internal Revenue Bureau, so far from being benefitted by the acts of retail druggists who refuse to handle intoxicating liquors for the filling of prescriptions, is likely to find itself somewhat embarrassed. It is greatly to the advantage of the Government that, inasmuch as intoxicants may lawfully be sold for medicinal purposes and therefore will be sold, they should be handled by the most reputable merchants in the country and that the traffic should not be turned over to persons of doubtful character. But does not every honest, high-minded retailer who, in any community, refuses to fill prescriptions for intoxicants assist in concentrating the business in the hands of a smaller number, some of whom may be less conscientious, and thus add to the difficulties experienced by the Internal Revenue Bureau in preventing abuses?

Furthermore, even assuming that there are none but honest and reputable druggists in a given community, and that, because there is no central dispensing system, a few of them conscientiously determine it to be their duty to shoulder this burden, is it not apparent that if the filling of all the local physicians' prescriptions for stimulants devolves upon a fraction of the number of the local druggists, their business will soon assume a character that will bring them under undeserved suspicion?

I regret that I cannot sympathize at all with those retail druggists who have refused to take out permits to handle or use non-beverage alcohol as distinguished from whiskey and other beverage forms of spirits. I cannot see how a modern pharmacy can be conducted without the use of alcohol. Of course, a retail druggist may become a peddler of toilet articles, tobacco, stationery, confectionery and soda water, but it seems to me that he must put his professional pride in his pocket and voluntarily scrap a large part of his education as a pharmacist when he decides that he will not use alcohol in any form. Pussyfooting should be beneath the dignity of men boasting a scientific training.

To my mind, the retail drug trade, in this connection presents a clear case of *noblesse oblige*. Because of the high standing of the educated pharmacist, individually and collectively, it is his duty to

assume, in addition to the ordinary burdens of citizenship, the extra load which his intellectual equipment and his special knowledge fit him to carry. He cannot conscientiously sidestep it nor impose it upon another.

If, therefore, you will shoulder your burdens like men and, like men, discharge your obligations to your trade and your country, you will earn the right, whenever your acts are called in question or whenever you find yourselves facing a difficult situation, to come to Washington and, in the tones in which real men speak, demand a square deal at the hands not only of the executive departments but, if necessary, of that august body the Congress of the United States itself.

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### MISSOURI PHARMACISTS' WORK AND PLAY.

The Missouri Pharmaceutical Association, the 'Travelers' Organization, the Ladies' Auxiliary, the Veteran Druggists and the Missouri Board of Pharmacy were all in convention at the Elms Hotel, Excelsior Springs, June 8-11.

The total attendance was over four hundred. About one hundred and fifty members of the Mo. Ph. A., over one hundred were salesmen and the rest families of members and salesmen, together with fifty candidates for registration.

This meeting in a greater degree than any previous meeting, was decidedly a commercial affair. Addresses, discussions and demonstrations reflected the problems of the average drug store of the day.

Ex-Senator J. Ham Lewis, of Illinois, discussed economic conditions of the world. The Missouri prohibition enforcement officer told the retailers what must be done in order to comply with the law. M. J. Ulber, manager of the Union Depot Store, at Kansas City, explained in detail the plan on which such a store is managed. Samuel C. Henry, General Secretary of the N. A. R. D., outlined the work being done by that organization. Delegates from the A. Ph. A., the St. Louis R. D. A. and other organizations reported. E. G. Binz, of Los Angeles, ex-President of the California Ph. A., reported very satisfactory business conditions on the coast.

Treasurer William Mittelbach showed a balance of \$857.48. Secretary H. M. Whelpley reported 772 members. Secretary H. C. Tindall, of the Board of Pharmacy, stated that Missouri had 5241 registered and 255 assistant pharmacists.

The papers presented included, "The 1895 Meeting," by H. M. Whelpley; "Is Your Druggist More than a Merchant?" by C. H. McDonald; "Veterinary Pharmacy," by D. V. Whitney, Jr., "What of the Day and What of the Future of Pharmacy," by H. M. Whelpley.

It was decided to continue *The Missouri Druggist* as a quarterly.

Excelsior Springs was selected for the 1921 meeting, the second Tuesday in June.

Pre-requisite legislation was again endorsed and the committee instructed to ask for such a law. Forty-two new members were elected. County organization is under way in Missouri and will be further pushed, this year. Don S. Freiday, president of the Oklahoma Ph. A., explained the progress of county organizations in his state.

The following resolution, introduced by Fred H. Swift and L. A. Seitz, was adopted.

"Believing that the Government committed a tactical error in 'wishing' the liquor business upon the retail druggist, we, therefore, do resolve, in the interest of law-enforcement and that the high standard of pharmacy may be preserved untarnished, to politely but very firmly decline the 'honor,' standing pat on the proposition that liquor should be distributed through the dispensaries owned, operated and controlled by the government."

Officers for the ensuing year were elected by the various organizations, as follows:

#### MISSOURI PHARMACEUTICAL ASSOCIATION.

President, Charles H. McDonald, of Rocky Comfort; Honorary President, H. C. Churchill, of Windsor; First Vice-President, Robert Lisch, of Springfield; Second Vice-President, Wm. E. Bard, of Sedalia; Third Vice-President, M. J. Ulber, of Kansas City; General Secretary, Henry M. Whelpley, of St. Louis; Treasurer, Wm. Mittelbach, of Boonville; Editor *Missouri Druggist*, Minnie M. Whitney, of Kansas City; Local Secretary, H. C. Tindall, of Excelsior Springs; Assistant Secretary, Samuel G. Becker, of St. Louis; Council—A. C. Smith (Chairman), of Carrolton; Minnie M. Whitney (Secretary), of Kansas City; Dr. Otto F. Claus, of St. Louis; R. A. Doyle, of East Prairie; H. D. Llewellyn, of Marshall.

MISSOURI PHARMACEUTICAL TRAVELERS' ASSOCIATION.

President, George Bennett, of Kansas City; First Vice-President, W. J. Walsh, of St. Louis; Second Vice-President, C. W. Loomis, of Kansas City; Third Vice-President, William O'Neil, of Chicago; Secretary, C. B. Wilkins, of Kansas City; Treasurer, Dan Liddy, of Kansas City.

LADIES' AUXILIARY.

President, Mrs. Charles Hose, of Kansas City; First Vice-President, Mrs. A. C. Smith, of Carrollton; Second Vice-President, Mrs. R. L. Hope, of Centralia; Third Vice-President, Mrs. C. B. Wilkins, of Kansas City; Recording Secretary, Mrs. C. P. Johnson, of St. Louis; Corresponding Secretary, Mrs. C. A. Peck, of Excelsior Springs; Treasurer, Mrs. C. W. Loomis, of Kansas City; Auditor, Mrs. Charles Schall, of St. Louis.

Six of those who organized the Mo. Ph. A. in 1879 were in attendance and held a reunion.

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THE FIFTIETH ANNUAL MEETING OF THE NEW JERSEY  
PHARMACEUTICAL ASSOCIATION.

The Golden Jubilee meeting of this Association was held in the city of Newark, June 7th to 11th. The initial meeting for the organization of this Association was held in the same city, February 17th, 1890. The session opened with the President's Reception at the Hotel Saint Francis on Monday evening. At the close of the reception, games and dancing were enjoyed by the members and their guests.

The business meetings and entertainments were held at Stetter's Auditorium on Broad Street, some distance away from the hotel headquarters. The first meeting on Tuesday morning was opened with an invocation and an address of welcome by the mayor of the city. A number of delegates were present representing sister State Associations, The National Wholesale Druggists' Association, The National Association of Retail Druggists, American Pharmaceutical Association, and a number of colleges and local Pharmaceutical Associations.

Several of the papers read were of historical interest, appropriate

to the celebration. Others were of a scientific character; noteworthy among these was the paper by R. G. Eccles, M.D., on the "Use of Drugs in Disease." Among the important reports presented were those of the Committee on Pharmacopoeas, Delegates to the Pharmacopoeial Convention, Legislation, and the several reports from the Board of Pharmacy.

The Board presented to the members a copy of the "Schedule of Antidotes for Poisons," which had just been issued as authorized by the amendment to the Pharmacy Law enacted the year prior. This presents in a very convenient form the approved antidotal treatment for the drugs and chemicals more likely to cause toxic effects. This is a commendable feature incorporated in the New Jersey Pharmacy Act. Copies of this schedule can be secured by addressing the Secretary, Edgar R. Sparks, Burlington, N. J.

The entertainment features were a noted portion of the celebration. The principle events were on Tuesday evening, a vaudeville entertainment and an illustrated lecture by Prof. Wm. Mansfield, of Albany, N. Y.; the reception at the home of Mrs. Charles Holzhauer on Wednesday evening; the travelling men's entertainment on Thursday evening; the field sports on the Newark Athletic Field; automobile ride to Newark Port and inspection of the captured German war relics; and an automobile country ride for the ladies with a stop at Washington's Headquarters at Morristown. These were the main entertainment features that were crowded into this busy week.

The Golden Jubilee banquet on Friday evening was the climax of the celebration. Mr. Wm. O. Kuebler was toastmaster, and the principle address of the evening was made by Judge Robert Carey. The surprise of the evening came in the nature of gifts presented to the retiring President, Edward A. Sayre, and to Harry W. Crooks, local Secretary and President-elect, in recognition of their efficient service in making the Semi-Centennial Celebration a grand success.

A memorial volume of 100 pages was prepared by President Sayre. This contained a short historical sketch of the Association, and brief memoirs and portraits of the Forty-eight men who had filled the presidential chair since the organization had been effected. This souvenir will doubtless be highly prized as commemorating the events of the Semi-Centennial session of this Association.

G. M. B.



## FORTY-THIRD ANNUAL CONVENTION OF THE PENNSYLVANIA PHARMACEUTICAL ASSOCIATION.

The forty-third annual convention of the Pennsylvania Pharmaceutical Association was held at Harrisburg, June 22 to 24, inclusive, and was one of the best attended and most enthusiastic conventions held in recent years. The Association not only accomplished a great deal by way of disposing of current issues, but inaugurated a program for future work, which contemplates great advances in the progress of pharmacy in Pennsylvania.

The convention was informally opened on Tuesday morning, June 22, by President Robert P. Fischelis.

The report of the Executive Committee referred to the necessity for increasing the annual dues in order to meet the expenses of conducting the business of the association and called attention to the death of eight members during the past year and the addition of one member to the life membership roll.

The Treasurer's report showed a balance of more than five hundred dollars in the current fund of the Association and about four hundred dollars in the invested funds.

Delegates were present from the New York State Pharmaceutical Association, Delaware Pharmaceutical Association, Philadelphia and Pittsburgh colleges of pharmacy and the various local associations throughout the State.

A communication received from Dr. Jacob Diner, Chairman of the Committee on Classifying Pharmacies of the American Pharmaceutical Association, caused some discussion and led to a motion that the Legislative Committee be instructed to draft a bill leading to classification of pharmacies into drug stores and professional pharmacies in Pennsylvania. This was referred to the Committee on President's Address, and that Committee later reported a recommendation to refer the matter to the Legislative Committee, with instructions to make a study of the subject and bring in a report at the next meeting, as to the propriety and feasibility of such legislative action. This recommendation was adopted.

A communication from Dr. E. L. Newcomb, of Minnesota, referring to a plan of increasing the membership in the national and state associations was read and referred to the Committee on President's Address, which later recommended that the initiative on this matter should be taken by the national organizations involved and when this has been brought about, the active support of the Pennsyl-

vania Pharmaceutical Association should be pledged. This recommendation was adopted.

At the second session of the convention Mr. Eugene C. Brockmeyer, General Counsel of the National Association of Retail Druggists, delivered an address on national legislation and the rôle which the pharmacist should play in securing adequate recognition for his calling.

Mr. Brockmeyer dwelled on the organization of a committee consisting of one pharmacist from each state, which would interview candidates for the state and national legislatures on subjects in which pharmacists are interested, so as to determine in advance what the attitude of these men would be on matters affecting pharmacy.

He pointed out that the American Medical Association and other associations had firmly entrenched themselves in years gone by and were now in a position to handle their legislative matters much more easily than do the pharmaceutical associations. Mr. Brockmeyer referred to the excellent opportunity pharmacists have for influencing members of their communities and through them, members of Congress on legislation, that will benefit the public as well as pharmacists. At the conclusion of his remarks Mr. Brockmeyer was given a rising vote of thanks and answered a number of questions that were asked from the floor.

The report of the Committee on Patents and Trade Marks was then read by Dr. F. E. Stewart and dealt largely with the aspirin case that is now pending in the courts of New York.

This was followed by a report of the Committee on Botany read by Dr. Adolph W. Miller which contained many scientific and practical references to the progress of botany.

The third session of the convention opened Tuesday evening at 8 P.M. in the ballroom of the Penn-Harris Hotel and this was the formal opening of the convention. Rev. S. W. Herman, of Harrisburg, offered prayer, after which President Fischelis introduced Mayor Hoverter of the city of Harrisburg, who welcomed the members on behalf of the citizens of that city. His address of welcome was responded to by Dr. L. L. Walton of Williamsport, on behalf of the Association, and by Mrs. David McMurtrie on behalf of the ladies.

The President then called First Vice-President H. J. Mentzer to the chair while he read his annual address. This was a valuable

résumé of the important events and legislation affecting pharmacy that had transpired during the year. It contained many valuable suggestions, which are fully covered in the report of the Committee on President's Address.

At the fourth session the report of the Committee on Drug Market was read by John G. Roberts, Chairman, and contained many valuable contributions on the quality of drugs and chemicals now being obtained from foreign and domestic sources.

P. S. Rohn, of Philadelphia, was then called upon to present the report of the Committee on Membership, and his statement that 350 new members had been taken into the association in the past year was roundly applauded.

Dr. H. V. Army addressed the convention on the subject of Research in American Pharmacy. Dr. Army complimented the Pennsylvania Pharmaceutical Association on the active part it has always taken in the development of American Pharmacy and the great amount of research work carried on by its members. He pointed out the many important discoveries in chemistry, pharmacy and allied sciences which had been made by pharmacists working in their laboratories and called attention to the great field of work still before us. This address was highly complimented by various members.

Lieutenant Havinghurst of the United States Army was then called upon to deliver a message on the new Peace-time Army. He pointed out the difference between the regular army of pre-war days and the new army that was now being organized and the wonderful opportunities offered young men for securing not only military training but an education in various crafts.

The President then introduced Hon. J. H. Divel, of Philadelphia, from the office of the Prohibition Director, who spoke at some length on the problem confronting his office in carrying out the enforcement of the prohibition law.

Mr. Divel pointed out the great influence that the pharmacists of the State wield with the community at large and called for their wholehearted coöperation in enforcing the 18th amendment and the Volstead Law. He then offered to answer any questions that might be propounded by the members on the subject of prohibition legislation and a very interesting discussion ensued. This was followed by a motion by Mr. Heffner, of Lockhaven, that a committee of five be appointed to take up with Mr. Divel the matter of prohibi-

tion enforcement and prepare resolutions to be sent to Congress, expressing the attitude of the association on a number of questions concerning the law. The matter was disposed of by referring consideration of the subject to the Association's Committee on Legislation.

The entire afternoon of this day was spent at Hershey, Pa., inspecting the grounds and buildings of the Hershey Chocolate Company, and the members of the Association were the guests of the Hershey Company at a dinner served in one of the pavilions at Hershey, after which the annual entertainment of the Travelling Mens' Auxiliary was held at the auditorium.

The fifth session of the convention was held on Thursday morning, June 24, and was devoted almost entirely to the reading and discussion of papers. The Committee on Papers and Queries headed by Mrs. Charles H. LaWall as Chairman, had been active throughout the year and had secured about 40 papers for this meeting. Lack of time prevented reading all of them, but practically all who were present during the session of the committee and had written papers were given an opportunity to read them.

At 11 o'clock the President announced that Dr. Edward Martin the State Commissioner of Health, had come over from the Capitol to address the members and then introduced Dr. Martin.

In a short address the Commissioner paid a splendid tribute to the Association for the coöperation that had been given him by the pharmacists of the State in all Public Health Measures. He outlined some of the problems now before the department. In doing so, he pointed out where the pharmacists could be of help in each case. His remarks made a profound impression upon the members and at their conclusion, Professor LaWall in rising to thank the Commissioner for his address, also moved that he be made an honorary member of the Association. This motion was carried unanimously with a rising vote.

It is the first time that the Pennsylvania Pharmaceutical Association has elected more than one honorary member in any one year and also the first time that a State Official has been so recognized.

The sixth session of the convention was called to order at 2 P.M., Thursday afternoon, June 24, and Dr. L. L. Walton, of Williamsport, the Chairman, presented the annual report of the Committee on Legislation. Dr. Walton reported that the committee had not been very active during the year, because of the fact that the State Legis-

lature had not been in session. He reported on several phases of National legislation and pointed out what progress had been made for preparing for the next session of the State Legislature.

Following this report Mr. Charles Rehfuß, of Philadelphia, introduced a resolution asking for the appointment of a committee of five retail druggists to take up all matters referring to prohibition legislation with the Prohibition Commissioner's office.

This committee is also to become a part of the Committee on Legislation when State legislation on the alcohol situation is considered. The resolution was passed.

Dr. Walton also reported for the Pennsylvania Board of Pharmacy of which he is the Secretary. In a very interesting manner he pointed out some of the problems with which the Board has to contend and quoted some correspondence on various subjects to show the wide range of activity and the great mass of detail handled by the Secretary's office.

The report of the Committee on President's Address was then presented by the Chairman, Professor Charles H. LaWall, as follows:

#### REPORT OF THE COMMITTEE ON PRESIDENT'S ADDRESS.

Your Committee on President's Address in submitting this report upon the matters referred to them, wish to express the unanimous opinion that the address of President Fischelis is worthy of the highest traditions of the office, and both in form and substance is to be commended for its clarity, its comprehensiveness and its progressiveness.

Its recommendations give evidence of careful constructive planning for the welfare of the organization, and are worthy of, and have been given, most careful consideration.

Taking them up in the order of their presentation we unanimously voice the following opinions upon the respective subjects:

#### FINANCES.

The growing costs of administration coupled with the growing needs of our association make it imperative that something should be done to augment our finances. We, therefore, approve of the proposal that our by-laws shall be amended so as to increase the annual dues from two to three dollars, this change to take effect when the dues for 1921 are collected.

We believe, however, that there are certain inherent advantages

in maintaining a treasurer as a distinct office from the Secretary, and we do not approve of the proposal to amend the constitution so as to enable these offices to be combined.

#### R. L. D. CLASSIFICATION.

We heartily endorse the proposal to join with other State and National Pharmaceutical Organizations in a concerted effort to relieve pharmacists of the stigma of being called Retail Liquor Dealers when they are not so in fact, and approve the recommendation that the Committee of Legislation of this Association be authorized to coöperate in the drafting and passing of suitable legislation to accomplish this aim.

#### COMPULSORY HEALTH INSURANCE.

We approve of the recommendation that the Legislative Committee of the P. P. A. be instructed to wage an active campaign against Compulsory Health Legislation, and to coöperate toward this end with all other organizations working for this same purpose.

#### STATE PHARMACEUTICAL EXPERIMENT STATION.

We approve of the recommendation that the Legislative Committee of this Association be authorized to draw up and have introduced into the next legislature, a bill providing for the establishment of such an institution which should be modeled upon the lines of the Wisconsin station, and that the incoming officers be requested to inaugurate an active, educational campaign leading to the accomplishment of this plan.

#### ADVISORY COUNCIL REPRESENTATION IN HEALTH DEPARTMENT.

We approve of the recommendation that we endorse by appropriate resolution the sympathetic attitude of the Pennsylvania Department of Health under the able leadership of Dr. Edward Martin, and that a request be made for the appointment of a Pharmaceutical representative upon the Advisory Council of the Health Department. We further feel that such a request should be accompanied by a list of five prominent pharmacists, members of this Association, eligible for appointment to such position, and that this list should be selected by the Executive Committee of the Association.

#### METRIC SYSTEM OF WEIGHTS AND MEASURES.

We emphatically approve the universal adoption of the metric system for all commercial transactions at as early a date as is prac-

licable, and that notice of such approval be sent to our Congressman, the American Metric Association and the World Trade Club.

#### THE PUBLICATIONS OF THE ASSOCIATION.

The fullest and freest independent action and development of an organization are best stimulated by its control of its own publications. Although the increase in the annual dues would enable the offer of one of the two outside publications from whom proposals have been received to take over a great portion of our publication work, we believe that it would be inadvisable at this time to make any definite arrangements with either of these journals. We recommend, therefore, that the publication of the *Pennsylvania Pharmacist* be continued in amplified form, so as to bring about its development as an invaluable asset to our work.

#### PUBLICITY.

We approve of the recommendation that our Committee on Publicity be authorized to coöperate with the Drug Trade Board of public information, and that a minimum appropriation of \$100.00 be made in furtherance of this aim, with such additional aid as may be found necessary, if approved by the Executive Committee.

#### NATIONAL ASSOCIATION OF RETAIL DRUGGISTS.

We approve of the recommendation that we continue our active affiliation with this Association, and that the customary payment of \$25.00 be made for membership.

#### PENNSYLVANIA MERCHANTS' ASSOCIATION.

We approve of the recommendation that three delegates again be appointed to represent our Association at the annual meeting of this organization, and that our coöperation be offered along lines leading to the improvement of merchandizing conditions.

#### HONORARY MEMBERSHIP.

We heartily approve of the proposal to add the name of Professor H. V. Army to the list of our Honorary Members. His prominence and activity in American Pharmacy make such recognition of his services both timely and fitting.

#### MEMORIAL SESSION.

We approve of the recommendation that a time be set aside for a short memorial session in honor of those who have died during the past year. We suggest that such a session be held immediately

after reading the minutes at the opening of the final session on Thursday evening; and also approve of the proposal to have the Secretary include photographs of the prominent association workers among the deceased in our next annual proceedings.

In the report of the delegates to the Pennsylvania Medical Society, the recommendation was made that this Association go on record as favoring the work of the Council on Pharmacy and Chemistry of the American Medical Association, and that the Secretary send official notice of such action to the Association. We unanimously endorse this suggestion.

In concluding this report for formal presentation and action, we wish to impress upon the members that certain very radical changes have been authorized, and that the incoming officers be duly impressed with the necessity of immediately inaugurating such a publicity campaign through the columns of the Pennsylvania Pharmacist and otherwise, as will minimize the possible loss in membership through the raising of the dues.

It will be the twentieth anniversary next year of the occasion of lowering the annual dues from four dollars to two dollars. Surely our Association during these years of activity has more than justified the necessity of only a partial return to the former figure. "Less than a cent a day" is a catch phrase used in the President's address which might be used to good effect in this connection.

The report of the Committee was approved in its entirety and the President then called for the report of the Committee on Nominations, which was presented by J. C. Peacock, the Chairman, as follows:

For President, W. J. Sturgeon, of Kittanning.

First Vice-President, W. B. Goodyear, of Harrisburg.

Second Vice-President, J. N. G. Long, of Philadelphia.

Secretary, Louis Saalbach, of Pittsburgh.

Treasurer, F. H. E. Glein, of Lebanon.

Local Secretary, Ambrose Hunsberger, of Philadelphia.

Member of the Executive Committee for three years, the retiring President, Robert P. Fischelis.

The report of the Committee was received, unanimously approved and the nominees were declared elected to the offices for the ensuing year.

The seventh session of the convention was held Thursday evening at 8 P.M., and was featured by an illustrated lecture, entitled "Who's Who in the P. P. A.," by Professor Charles H. LaWall.



The lecturer had prepared at considerable expense and trouble a large number of lantern slides of past and present members of the Pennsylvania Pharmaceutical Association, who had been active in the conduct of its affairs. These slides were taken from portraits and also from snapshot photographs, and the remarks of the speaker regarding the various personalities shown combined with the slides themselves made a very entertaining address.

After the installation of the officers the meeting adjourned to reconvene for the forty-fourth annual convention in Philadelphia next year, at the time of the Centennial Celebration of the Philadelphia College of Pharmacy.

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## COMMENCEMENT OF THE PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE.

The Ninety-Eighth Annual Commencement Week of the Philadelphia College of Pharmacy and Science began with the Baccalaureate services held in the Church of St. Luke and the Epiphany, Sunday, May 30th, at 4 o'clock. The Rev. David M. Steele was the Baccalaureate preacher.

On Monday afternoon, May 31st, the Annual Meeting of the Alumni Association was held in the College building and was unusually well attended. President Robert P. Fischelis in his annual report sounded the keynote of the campaign for a greater College of Pharmacy. He pointed out that the charter of the College had been changed, so as to permit the granting of degrees in the various sciences, and that the name of the institution had been changed from Philadelphia College of Pharmacy to Philadelphia College of Pharmacy and Science.

He referred to the work of the Alumni Association during the year and pointed out that arrangements had been made to secure a memorial tablet in honor of the graduates and students of the College who served in the World War and in special recognition of those who made the supreme sacrifice.

He announced that the Alumni Association was on a better financial footing than it had ever been before, and that the nucleus of an endowment fund for the work of the Alumni Association alone had been started by the purchase of a \$1000 Liberty Bond. He urged the Alumni of the College everywhere to lend their aid in the

coming campaign for endowment and buildings, to be conducted by the College.

Professor Clement B. Lowe, Chairman of the Committee on Necrology, reported that 59 members of the Association had died during the year, among them Frank G. Ryan, of the Class of 1884, who had been president of the Parke Davis Company for a number of years.

The following officers were elected for the ensuing year:

President, Wm. Duffield Robinson, M.D., '76

First Vice-President, Russell T. Blackwood, '91.

Second Vice-President, M. M. Smith, '13.

Corresponding Secretary, Ivor Griffith, '12.

Treasurer, Wm. H. Gano, '84.

Board of Directors—Mrs. Charles H. LaWall, '04; Dr. P. S. Pittenger, '09; Mrs. J. C. Peacock, '96; Dr. Mitchell Bernstein, '09; Dr. Eugene G. Eberle, '84.

Mr. Samuel C. Henry, Secretary of the N. A. R. D., was elected honorary member of the Alumni Association.

The Professors' and Trustees' supper to the graduating class was held in the Museum of the College Monday evening, May 31st, Dean Charles H. LaWall, presiding. Brief addresses were made by President Howard B. French, of the College, members of the Faculty and a number of the graduates.

The Annual Reunion and Banquet of the Association was held at Mosbach's Casino, Tuesday evening, June 1st, and more than 200 Alumni of the College turned out for this affair. Dr. Robert P. Fischelis, the retiring President of the Alumni Association, was the toastmaster. President Howard B. French, in his address, told of the two million dollar endowment and building campaign which the College was about to undertake and showed the first architect's drawings of the proposed College buildings on the Philadelphia Parkway.

Mr. French announced that the Park Commission was favorably inclined toward granting a site for the College and that the plans which are now maturing provide for a plant consisting of six buildings which will house the various departments of the College and also provide ample facilities for research work.

Other speakers at the banquet were Dean Charles H. LaWall, Dean J. W. Sturmer, Professor E. Fullerton Cook, and members of the quinquennial reunion classes.

One of the features of the reunion and banquet was the unveiling of the memorial tablet in honor of the graduates and students of the College who had been in the service. Dr. Wm. Duffield Robinson, the President-elect of the Alumni Association, made the address in connection with the unveiling, and Miss Ruth Ernestine Cook, daughter of Prof. Cook, unveiled the tablet.

The 98th Annual Commencement wound up the activities of the week and was held at the American Academy of Music, Broad and Locust Streets. Prayer was offered by Rev. J. Gray Bolton, and the address to the graduating class was made by the Hon. John Wanamaker. The honorary degree of Master in Pharmacy was awarded to Dr. Frederick B. Kilmer, of New Brunswick, N. J., and Dr. Francis E. Stewart, of Philadelphia. The College prizes were awarded by members of the Faculty and Board of Trustees, the awards being read by Dean LaWall and the Alumni prizes presented by Dr. Robert P. Fischelis, the retiring President of the Alumni Association.

The list of graduates in the various courses follows:

#### GRADUATING CLASS.

##### NINETY-EIGHTH SESSION.

1919-1920.

#### BACHELOR OF SCIENCE IN PHARMACY AND CHEMISTRY (B.Sc.).

Name.	Thesis.	Where From.
Slothower, George.....	<i>Rhus venenata</i> .....	Pennsylvania
Slotter, Charles Franklin.....	Studies on Commercial Varieties of <i>Nux Vomica</i> .....	Pennsylvania

#### DOCTOR IN PHARMACY (P.D.)

McNelis, Miss Anna Camillus (P.C.).....	<i>Ampoules</i> .....	Pennsylvania
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#### BACHELOR IN PHARMACY (PHAR.B.).

Buehler, Luther Alexander.....	<i>Japan Wax in Ointments and Cera's</i> .....	Pennsylvania
Reighter, William Erle.....	<i>Tablet Triturates</i> .....	Pennsylvania

#### PHARMACEUTICAL CHEMIST (PH.C.).

Marxuach, Acislo.....	<i>Bixa Orellana</i> .....	Porto Rico
Randolph, John Roanoke.....	<i>Composition of Manganese Dioxide, U. S. P.</i> .....	Missouri

Name.	Thesis.	Where From.
Steves, Bertram Clarence.....	<i>The Saponification of Fats with Alkali Carbonates.</i> .....	New York
Steward, Charles Robert.....	<i>The Relative Sensitiveness of Some of the Tests Used in the Detection of Dextrose in Urine.</i> .....	Idaho

## GRADUATE IN PHARMACY (PH.G.).

Abrahamson, Oscar.....	<i>Modern Merchandising.</i> .....	Pennsylvania
Aidenbaum, Philip Lincoln.....	<i>Retail Drug Store Advertising.</i> .....	Pennsylvania
Bell, Harry.....	<i>Alcohol.</i> .....	Pennsylvania
Berman, Benjamin.....	<i>Economic Lichens.</i> .....	Virginia
Best, Elton McCoy.....	<i>Mercurochrome 220.</i> .....	N. Carolina
Bloomfield, Morris.....	<i>Glyceride Tinctures.</i> .....	Pennsylvania
Bornstein, Miss Rebecca.....	<i>Sponges.</i> .....	Florida
Bricker, Chester William.....	<i>Tolu as a Coating for Pills.</i> .....	Pennsylvania
Brown, Russell Leo.....	<i>The Cut-Rate Drug Store.</i> .....	Pennsylvania
Buch, Harry Harris.....	<i>Blood Transfusion.</i> .....	Pennsylvania
Budin, Barnett.....	<i>A Better Extract of Coffee.</i> .....	Pennsylvania
Burton, Robert Jefferson.....	<i>Non-Alcoholic Flavors.</i> .....	Pennsylvania
Byers, Wayne Emmanuel.....	<i>The Pharmacological Studies of the Ipecac Alkaloids.</i> .....	Pennsylvania
Carstater, James Cowling.....	<i>Compressed Tablets.</i> .....	Pennsylvania
Coffman, Charles Wayne.....	<i>Chamois Skins.</i> .....	Pennsylvania
Cohen, Mrs. Hassie D. G.....	<i>Fluidextract of Bitter Orange Peel.</i> .....	Pennsylvania
Coleman, David.....	<i>Cold Cream.</i> .....	Pennsylvania
Cramer, Richard Edward.....	<i>Virus Vaccinicum.</i> .....	New Jersey
Daly, Thomas Joseph.....	<i>Dichloramine T and Its Allied Products.</i> .....	Pennsylvania
Delle, Walter Hughlee.....	<i>Variations of the Teaspoon.</i> .....	Pennsylvania
Derick, George Coyle.....	<i>Reducing the Alcohol in Tinctures.</i> .....	Pennsylvania
Dry, Robert Levi.....	<i>Prescription Filling and Incompatibilities.</i> .....	Pennsylvania
Edge, Nicholas Joseph.....	<i>Mercurochrome 220.</i> .....	Pennsylvania
Fenton, Percival Norman.....	<i>Benzyl Benzoate and Ways of Administration.</i> .....	New Jersey
Flaherty, Richard Cyril.....	<i>A Commercial Source of Tragacanth and Detection of Its Adulterant.</i> .....	Pennsylvania
Fleisher, Joseph Charles.....	<i>Insecticide—Their Preparations and Applications.</i> .....	Pennsylvania
Forman, Joseph Maurice.....	<i>Hydrocyanic Acid Gas.</i> .....	Pennsylvania
Furman, Frank Hagenbuch.....	<i>Buchu Leaves and Adulterants.</i> .....	Pennsylvania
Galloway, Clarence Moore.....	<i>The Microscope—A Scientific Adjunct to Pharmacy.</i> .....	Pennsylvania
Gold, Maurice George.....	<i>Histology of Cocillana Bark.</i> .....	Russia
Green, Samuel.....	<i>Streptococcus Hemolyticus and Its Significance in Diseases.</i> .....	Pennsylvania

Name.	Thesis.	Where From.
Haberstroh, Ambrose Rea.....	<i>Adulteration and Identification of Drugs.....</i>	Pennsylvania
Haines, Howard Jacob.....	<i>Liquid Petrolatum.....</i>	Pennsylvania
Hargreaves, Miss Lottie.....	<i>Assay of Commercial Varieties of Hydrogen Peroxide.....</i>	Pennsylvania
Hartman, Jennings Bryan.....	<i>Depilatories and Deodorants.....</i>	Pennsylvania
Harvey, John Parker.....	<i>Dental Drugs and Chemicals.....</i>	Ohio
Heckert, Paul Franklin.....	<i>Cane Sugar—History and Compo- sition.....</i>	Pennsylvania
Jacobs, Daniel LeRoy.....	<i>Drugs That Enslave.....</i>	Pennsylvania
Knouse, John Allan.....	<i>Compounding and Dispensing Rec- tal Suppositories.....</i>	Pennsylvania
Kramer, Nathan Henry.....	<i>The Antiseptic Flavine.....</i>	Pennsylvania
Kwiatkowski, Adam John.....	<i>Monohydrated Sodium Carbonate....</i>	Pennsylvania
Laskowski, Adolph Leon.....	<i>The Discoveries of Louis Pasteur....</i>	Pennsylvania
LaWall, William Harland.....	<i>Intestinal Parasites.....</i>	Pennsylvania
Lowenthal Joseph.....	<i>My Experience in an Italian Drug Store.....</i>	Pennsylvania
McCauley, William Aloysius....	<i>Ambrine.....</i>	Pennsylvania
McGavin, John Thomas.....	<i>Pollination of Plants.....</i>	Pennsylvania
McWilliams, Lester Mahlon....	<i>Benzyl Benzoate.....</i>	Pennsylvania
Manus, Joseph.....	<i>The Amount of Alkaloids in Va- rious Preparations of Elixir Iron, Quinine and Strychnine.....</i>	Pennsylvania
Martin, Reuben Kaufman.....	<i>Arsenic—Its Toxicology and Ther- apeutics.....</i>	Pennsylvania
Martinez, Miss Matilde.....	<i>Dioscorea.....</i>	Cuba
Mear, James Frederick.....	<i>Manufacture of Pottery.....</i>	Ohio
Merklee, Benjamin Franklin...	<i>Cochineal.....</i>	Pennsylvania
Miller, John Harold.....	<i>Acriflavine.....</i>	Pennsylvania
Moran, Miss Rose Mary.....	<i>Drug Store Advertising.....</i>	Pennsylvania
Motley, Ferdinand.....	<i>Mercury (Historical).....</i>	New Jersey
Moyer, Irvin.....	<i>Manufacture of Perfumes.....</i>	Pennsylvania
Mutchnick, David Samuel.....	<i>Apothesine—Local Anesthesia.....</i>	Pennsylvania
Myers, William Bryan.....	<i>Helleborus Niger.....</i>	Pennsylvania
Nauman, Roy Augustus.....	<i>Effect of Prohibition on Medicines...</i>	Pennsylvania
Neiffer, Grover Wellington....	<i>Poisons and Their Antidotes.....</i>	Pennsylvania
Nicholl, Ellwood Ervin.....	<i>Show Windows.....</i>	Pennsylvania
Oswald, Anthony Cyril.....	<i>Hyoscyamus.....</i>	New York
Pawling, William Luther.....	<i>Sugar—Its Sources and Commer- cial Manufacture..</i>	Pennsylvania
Peters, Cyrus Adam.....	<i>Spiritus Aetheris Nitrosi.....</i>	Pennsylvania
Pine, Lynwood Carleton.....	<i>Possible Sources of Potash.....</i>	New Jersey
Rebarber, Isidor.....	<i>Microscopical Differences in Strqm- onium Leaves and Its Adulterant, Xanthium Strumarium.....</i>	New York

Name.	Thesis.	Where From.
Reber, Robert Elmer. ....	<i>Vulcanization of Rubber</i> .....	Pennsylvania
Reese, Charles Christian.....	<i>Celluloid</i> .....	Pennsylvania
Redinger, Lawrence Ernest.....	<i>Assay of Aspirin</i> .....	Pennsylvania
Rice, Miss Irene Esther.....	<i>Douglas Balsam of Fir</i> .....	Pennsylvania
Roatch, Karl Hobart.....		Pennsylvania
Rose, Herbert Leon.....	<i>Cultivation of Camphor and Its Home Economics</i> .....	Delaware
Ruplis, John Albert. ....	<i>Phenolphthalein</i> .....	Pennsylvania
Sachs, Samuel Frederick.....	<i>Toilet Lotions With Benzoin</i> .....	Maryland
Schaefer, Joseph William.....	<i>The Deterioration of Ethyl Nitrite Content in Spirit of Nitrous Ether</i> .....	Pennsylvania
Schaeffer, Charles Raymond...	<i>The Cascara Industry in the United States</i> .....	Pennsylvania
Schampan, Alexander.....	<i>Fluidextract of Conium</i> .....	Pennsylvania
Search, George Bruce.....	<i>Veronica Officinalis</i> .....	Pennsylvania
Seiple, Thomas Chester.....	<i>Glycerinum U. S. P.</i> .....	Pennsylvania
Seitzinger, William Oscar.....	<i>Industrial Uses of Ethyl Alcohol</i> .....	Pennsylvania
Senkowski, Ladislaus Anthony.	<i>Olive Oil and Its Manufacture</i> .....	Pennsylvania
Senseman, William Thomas....	<i>The Vulcanization of Rubber</i> .....	Pennsylvania
Shorr, Orrin.....	<i>Hydrocarbon Salicylate</i> .....	New Jersey
Sidler, Miss Mae Jennison....	<i>Ballota Nigra Adulterant</i> .....	Pennsylvania
Simpson, Ernest Biddle.....	<i>Vanilla and Its Preparation (Tincture N. F.)</i> .....	Pennsylvania
Smith, Frank MacFarland.....	<i>Soft Soap</i> .....	Pennsylvania
Smith, Samuel Lester.....	<i>Toluene</i> .....	Pennsylvania
Spencer, Lorange Robert.....	<i>Advertising</i> .....	Pennsylvania
Sukonick, Louis.....	<i>Hydrogen Dioxide</i> .....	Russia
Sutty, Arthur Paul.....	<i>Poison Gases and the Method of Testing Canisters for Efficiency Against Them</i> .....	Massachusetts
Swavely, Leon William.....	<i>Tincture of Cardamom</i> .....	Pennsylvania
Tamayo, Miguel Ocroa.....	<i>Picramnia Pentandra</i> .....	Cuba
Vogel, Mrs. Mary Lynch.....	<i>Practical Disinfection in the Sick Room</i> .....	Pennsylvania
Weidman, Isaac Snader.....	<i>The Influenza Bacillus</i> .....	Pennsylvania
Weinberg, Isadore Thomas....	<i>Spiritus Aetheris Nitrosi</i> .....	New Jersey
Weinberg, Maurice.....	<i>Barium Sulphate</i> .....	Pennsylvania
Weisbard, Leonard.....	<i>Physico Therapy Quackery</i> .....	Pennsylvania
Weise, Frank Herman.....	<i>Grindelia</i> .....	Idaho
White, Walter Williams.....	<i>Argyrol</i> .....	Pennsylvania
Wible, Hollis McCarrell.....	<i>The Presence of Boric Acid and Borax in Commercial Talcum Powders</i> .....	Pennsylvania
Wien, Stuart Eugene.....	<i>A French Pharmacy</i> .....	Pennsylvania
Wilson, Morris Faust.....	<i>Alcohol, Next to Water, the Most Valuable Chemical</i> .....	Pennsylvania

Name.	Thesis.	Where From.
Worrall, Wesley.....	<i>Ichthyol</i> .....	Pennsylvania
Young, Harry Blake.....	<i>Cork</i> .....	Pennsylvania
Zook Carl Elliott.....	<i>Veratrum Viride vs. Symplocarpus</i> <i>Foetidus</i> .....	Pennsylvania

STUDENTS WHO HAVE COMPLETED THE COURSE AND WILL  
RECEIVE THEIR DIPLOMA UPON REACHING THEIR MAJORITY.

Antes, Oliver Henry.....	<i>Atmospheric Fractionation</i> .....	Pennsylvania
Benedetti, Carlos Manuel.....	<i>Notes on Solanum Dulcamara</i> .....	Panama
Brown, Edwin Tyson.....	<i>Stable and Palatable Emulsions of</i> <i>Benzyl Benzoate</i> .....	Pennsylvania
Cantarow, Miss Rose.....	<i>Cork</i> .....	Connecticut
Freeman, Lewis Good.....	<i>Saturated Solutions</i> .....	Pennsylvania
Johnson, Charles Emerson.....	<i>Elaeagnus Longpipes</i> .....	New Jersey
Keuper, Joseph Thomas.....	<i>Organization of the Pharmacists in</i> <i>a Small City</i> .....	New Jersey
Kramer, Matthew.....	<i>Drosera, N. F.</i> .....	Pennsylvania
McAllister, Lory Curley.....	<i>Serum and Vaccine Therapy</i> .....	Pennsylvania
Martinez, Miss Carmen	<i>Convolvulus Scammonia and</i> <i>Ipomea Orizabensis</i> .....	Cuba
Moore, Clair Channell.....	<i>Manufacture and Uses of Pyralin</i> ...	Pennsylvania
Shenk, Robert William.....	<i>Salvia Triloba vs. Salvia Officinalis</i>	Pennsylvania
Widman, Lester Francis.....	<i>Althaea</i> .....	Pennsylvania

STUDENTS WHO HAVE COMPLETED THE COURSE AND ARE  
ELIGIBLE FOR THE DEGREE OF GRADUATE IN PHAR-  
MACY WHEN OTHER GRADUATION RE-  
QUIREMENTS SHALL HAVE  
BEEN MET.

Aument, Harry Groff.....	<i>Paraffin Dressings</i> .....	Pennsylvania
Bleeden, Miss Rose.....	<i>The Manufacture of Brushes</i> .....	Pennsylvania
Cline, Hubert Lee.....	<i>Assaying Phosphoric Acid</i> .....	Pennsylvania
Greeninger, Miss Florence	<i>Minerva</i> .....	Pennsylvania
Hoey, Miss Helen Lanning.....	<i>The Exit of Alcohol in Pharmacy</i> ...	Pennsylvania
Jaeger, Miss Marie Gertrude...	<i>The Evolution of Certain Pharma-</i> <i>ceuticals</i> .....	Pennsylvania
Koch, Charles Nicholas.....	<i>Biological Products</i> .....	Pennsylvania
Kurz, William Rabold.....	<i>Cotton</i> .....	Pennsylvania
Law, Harold Noble.....	<i>Ichthyol</i> .....	Pennsylvania
Leh, William Jennings Bryan...	<i>Making Soap from Olive Oil That</i> <i>Has Been Used in the Prepara-</i> <i>tion of Nuts</i> .....	Pennsylvania
Leigh, Francis Bernard.....	<i>Modern Pharmacies</i> .....	New Jersey

Name.	Thesis.	Where From.
Manus, Richard.....	<i>The Making of Syrup of Wild Cherry by Maceration.....</i>	Pennsylvania
Pitt, Charles Henry.....	<i>The Manufacture of Ethyl Nitrite...</i>	New Jersey
Raymond, Henry Simon.....	<i>Fluid Extract Conium.....</i>	Pennsylvania
Reeves, Miss Joanna Stretch...	<i>Sphagnum Moss, a Substitute for Cotton as a Surgical Dressing.....</i>	New Jersey
Roth, Herbert Joseph.....	<i>Rennet.....</i>	Pennsylvania
Seraballs, Enrique Aulet.....	<i>Psidium Pomifer.....</i>	Porto Rico
Starkey, Isaac Wayne.....		N. Carolina
Vidaurreta, Saturnino.....	<i>Colloids.....</i>	Honduras
Weidemann, Warren Rawson.	<i>An Examination of Solanum Nigrum Leaves.....</i>	Pennsylvania
Zapp, Mathias Augustus.....	<i>Senecio Aureus.....</i>	Idaho

## CERTIFICATE OF PROFICIENCY IN CHEMISTRY.

Curtis, Thomas F.....	New Jersey
Harnly, Paul G.....	Pennsylvania
Kantner, Brooke Bryon.....	Pennsylvania
Murray, Allen Foster.....	Pennsylvania
Rickart, G. Emerson.....	Pennsylvania

## CERTIFICATE IN BACTERIOLOGY.

Bernstein, Miss Nita N.....	Pennsylvania
Bossart, Miss Ruth A.....	Pennsylvania
Buchanan, Raymond Joseph, Ph.G.....	Pennsylvania
Kahn, Charles.....	Illinois
Koenig, Otto L., Jr., P.D.....	Pennsylvania
Kopp, Raymond Harold.....	Pennsylvania
Little, Percy Hayden.....	Pennsylvania
Lubarsky, Abraham R., Ph.G.....	Pennsylvania
Moyer, Raymond J., P.D.....	Pennsylvania
Nicholl, Robert Milton.....	Pennsylvania
Rosenfeld, Lawrence Marx, P.D.....	Pennsylvania
Scott, John C.....	Pennsylvania
Sharadin, Ralph C., P.D.....	Pennsylvania
Steinel, Edward J.....	Pennsylvania
Tamplin, John S.....	W. Virginia
Van Norden, Miss Frances.....	New Jersey
Wetzel, Harry Woodall.....	Pennsylvania

## CERTIFICATE IN CLINICAL CHEMISTRY.

Friedman, William Leonard, Ph.G.....	Pennsylvania
Roatch, K. Hobart.....	Pennsylvania
Rosenfeld, Lawrence M., P.D.....	Pennsylvania
Sharadin, Ralph C., P.D.....	Pennsylvania
Tamayo, Miguel A.....	Cuba
Van Norden, Miss Frances.....	New Jersey



CERTIFICATE IN COSMETICS AND PERFUMES.

Name.	Where From.
Benedetti, Carlos Manuel.....	Panama
Hartman, Jennings Bryan.....	Pennsylvania
Seraballs, Enrique.....	Porto Rico

CERTIFICATE IN PHYSIOLOGICAL ASSAYING.

De Virgiliis, Arturo.....	Italy
Raymond, Henry Simon.....	Pennsylvania
Schaefer, Joseph William.....	Pennsylvania

CERTIFICATE IN TECHNICAL MICROSCOPY.

Goblewski, Alphonse.....	Pennsylvania
Steward, Charles Robert .....	Idaho

ADDRESS OF PRESIDENT R. P. FISCHELIS OF THE  
 ALUMNI ASSOCIATION OF THE PHILADELPHIA  
 COLLEGE OF PHARMACY. (In Abstract.)

As we meet to conduct the business of the fifty-sixth annual meeting of the alumni association of the Philadelphia College of Pharmacy, we are on the eve of the one hundredth anniversary of the founding of our Alma Mater and there loom up before us visions of an even greater future in the coming years than the wonderful advances which our college has made in the past century of its existence.

It is for us, the living and active alumni, to see to it that these visions of the future shall not end in the mere building of air castles but rather that we set out to accomplish them with an earnest purpose, enthusiasm and unbounded willingness to work so that in the years to come our followers may say of us as we now say of the founders of our college "They builded better than they knew."

If anyone had suggested to me five years ago that a graduate of the Medico-Chirurgical College might at some time become the president of the Alumni Association of the Philadelphia College of Pharmacy, I would probably have looked at him in blank amazement and wondered whether he was in his right mind, yet that seeming impossibility has become a reality. I cannot refrain from mentioning this fact because I doubt whether there ever was a merger of two rival institutions where such complete harmony has obtained among the respective alumni since the very beginning of

their Association. The pharmacy department of the Medico-Chirurgical College was the strongest department of that institution in many ways and its alumni, at the time, considered it a misfortune that circumstances, over which the department of pharmacy had not one iota of control, compelled its virtual abandonment and subsequent merger with the Philadelphia College of Pharmacy. However, the four years that have passed demonstrate clearly that although many of the traditions and individualities of the Medico-Chirurgical College have been submerged, as was of course inevitable, the spirit of the two institutions was so similar that the Medico-Chi graduates have found it comparatively easy to assume the rôle of alumni of the Philadelphia College of Pharmacy. Personally I can say that no more hearty support was ever accorded a president of the Medico-Chi Pharmacy Alumni Association by his fellow alumni than has been accorded me this year on the part of the Philadelphia College of Pharmacy alumni. I feel it is only just that this should be made a matter of record for I know that "Chi" alumni everywhere will consider it a compliment to them and will feel that their loyalty as adopted children of the Grand Old Mother Philadelphia College of Pharmacy is not for one moment misplaced.

We had a busy year and it is a pleasure to report that the Alumni Association has found it comparatively easy to resume its pre-war activities and in some instances enlarge upon them.

Everywhere about us there has been likewise a speedy resumption of peace-time activities. Although technically still at war, the country has long since turned its back upon the years of horror, which left their marks upon us all to a greater or less extent, and is looking forward to years of tranquility. But let us not forget too quickly the sacrifice of those who gave their all for the future happiness of the world. As I write these lines there comes to my mind a verse which on this memorial day is particularly appropriate:

"The tumult and the shouting dies;  
The captains and the kings depart.  
Still stands Thine ancient sacrifice;  
An humble and a contrite heart.  
Lord God of Hosts, be with us yet,  
Lest we forget! Lest we forget!"

We shall never forget the boys of the Philadelphia College of Pharmacy, nearly one thousand strong, who answered the call to the colors. A bronze memorial tablet to be erected in their honor

in the college building has been procured by the Alumni Association and will be dedicated at our annual reunion to-morrow evening. I want to express the thanks of the Association to the committee, consisting of Messrs. J. S. Beetem, W. H. Gano and F. P. Stroup, for their prompt and untiring efforts in making possible the dedication of this memorial to our alumni, who served and those who made the supreme sacrifice, at this early date. The funds required were made available by the contributors to the Alumni Sustaining Fund. Surely these contributors will feel proud to have made this lasting memorial to our boys possible.

Our college is to be congratulated on the enlargement of the scope of its charter. It is now legally, what it has long been practically, The Philadelphia College of Pharmacy and Science.

I recommend that the Board of Directors of the Alumni Association be empowered to change the name of the Alumni Association to correspond with the new legal title of the college and that our constitution and by-laws be so revised as to make them conform with the new name.

I further recommend that we establish two classes of membership in the Alumni Association, active membership and associate membership. Active members shall be those who graduate from any of the pharmaceutical or science courses of our college and have a degree conferred upon them. Associate members shall be those who attend and complete special courses in our college, for which no degrees are awarded but certificates are given. Associate members may be appointed upon standing or special committees of the Association but shall not have the right to vote or hold office, nor to occupy the chairmanship of committees.

The object of this recommendation is to include in the Alumni Association all former students of the college no matter what courses or partial courses they have taken and at the same time restrict the active management to those holding the degrees of the college. The latter procedure is necessary in my estimation in order to maintain the prestige of the college among institutions of the highest grade.

In years gone by, the Alumni Association depended in a large measure upon the college for its financial support. In the past two years an earnest attempt has been made to make the association self-sustaining. This is as it should be. So far we have depended entirely upon volunteers for our sustaining fund. This has resulted in placing the burden upon the few for the benefit of the many. I

would recommend fixing the annual dues of all members at 50 cents per annum with the proviso that no member shall ever be charged more than \$1.00 for arrears no matter how great his arrearage may be. This may not sound business-like at first but I am connected with an alumni association which has found this the most effective way of sustaining itself. The man who pays his dues regularly will hand you a dollar for two years dues whenever you let him know it is due and the fellow who ignores bills for five years and then becomes reticent about attending alumni reunions or college affairs because he is behind will feel happy when he is told he only owes \$1.00, and may become an active worker when under another system he would probably never go near the college again.

An Investment Fund has been started by the purchase of one \$100 Fourth U. S. Liberty Bond. Should any of our members desire to add to this fund by contributions of Liberty Bonds or cash in substantial amounts, either would be most gratefully received. The association officers are very desirous of securing an Investment Fund of \$10,000 in order to provide a regular source of income which will be most faithfully and carefully used to advance the interests and good-name of our century-old college. Of course, any contribution to the above-mentioned fund must be made without prejudice to any fund the college may endeavor to raise.

For the first time in a great many years the Alumni Association this year extended a formal welcome to the first year class of the college. A high grade entertainment was provided by the committee on reception and a splendid address by Hon. Franklin S. Edmonds featured the affair. Practically the entire class and a good representation of alumni attended. It is very important that incoming students be made to feel at home at the college and that the Philadelphia College of Pharmacy spirit be displayed to them at the earliest possible moment. I, therefore, recommend that a reception and entertainment by the Alumni Association to the incoming classes be considered as an annual custom and that it be held before Thanksgiving day each year.

It is a pleasure to note that eight alumni of the Philadelphia College of Pharmacy were elected to the Committee of Revision of the United States Pharmacopoeia at the recent Pharmacopoeial Convention, and it is still more gratifying for us that the high honor of being Chairman of this committee has again fallen to a Phila-

delphia College of Pharmacy graduate and a member of the college faculty, Prof. E. Fullerton Cook.

The centennial of the college has been alluded to before in this address. It is indeed a great event, for not only does it mark the one hundredth birthday of our college but also the one hundredth anniversary of the beginning of pharmaceutical education in America. The event must be celebrated as befits an occasion so auspicious and so far reaching in interest.

For a number of years it has been suggested that the college would soon acquire a site on the Philadelphia Parkway upon which new buildings could be erected. This site was to be the gift of the City of Philadelphia. In order to ascertain how the Alumni Association might be of help in this matter, a special meeting was called last fall of the Board of Directors of the alumni which was attended by President French and Mr. George M. Beringer, the chairman of the Board of Trustees. The chief development growing out of this meeting was the appointment of an alumni committee to assist in securing a site for the college. It had been clearly brought out at the meeting that securing a proper site was the key to the program of expansion.

The committee we appointed has interviewed members of the Parkway Commission and has been advised that the possibilities of securing a site on the Parkway are at least fair.

I would like to see our Alumni Association go on record to the effect that we will undertake a campaign to raise the necessary money for a suitable site if the college authorities are unable to convince the city that such a site should be given to us free. I believe the Philadelphia College of Pharmacy has a perfect right to ask the municipality, the State and private individuals for money with which to build an institution that will be of constant service to the people of this country, but, ladies and gentlemen, we will also have to do some contributing ourselves. When the time comes it will be necessary for every alumnus of this college from the President down to the poorest member of the graduating class to "dig deep" and add according to his means to whatever fund we may have been able to collect from others. The combined funds no matter how much they may amount to will hardly be sufficient to do all that we can and want to do for pharmacy and for the people of this country through our great institution.

I am greatly in favor of having the alumni association provide some one definite thing toward the enlarged college, either a building, or a site, or the equipment of some part of the structure. Whatever it may be it should be in the name of the Alumni Association so that in the years to come, graduates may point with pride to this definite part of the college which they helped to provide.

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SUMMARY OF THE PROCEEDINGS OF THE 1920 MEETING  
OF THE AMERICAN CONFERENCE OF PHARMA-  
CEUTICAL FACULTIES.

BY THEODORE J. BRADLEY,

SECRETARY.

The Twenty-first Annual Meeting of the American Conference of Pharmaceutical Faculties was held at the New Willard Hotel, Washington, D. C., on May 5-6, 1920. Delegates were in attendance from thirty-three member colleges located in twenty-five states. The President, Dr. Wortley F. Rudd, of the Medical College of Virginia School of Pharmacy, presided at all sessions.

After the roll-call of delegates, Professor John Uri Lloyd, of Cincinnati, opened the meeting with a message of greeting from the American Pharmaceutical Association.

Dr. Rudd's presidential address was well worked out and cordially received, and it contained several recommendations which were adopted as follows:

1. That the Conference take steps to secure an investigation and classification of the pharmacy schools of the United States.
2. That the Conference coöperate with the American Pharmaceutical Association and the National Association of Boards of Pharmacy to secure pre-requisite laws in states which have not yet enacted such laws.
3. That the President, Secretary-Treasurer and Chairman of the Executive Committee shall act as a special committee to secure publicity for the work of the Conference.
4. That the President, Secretary-Treasurer and Chairman of the Executive Committee shall hold a meeting in advance of the annual meeting, at the expense of the Conference, if these officers deem such a preliminary meeting necessary.

5. That the minimum course leading to a degree from a member college in the Conference shall be three years, beginning with the class entering in 1925.

Dr. C. C. Pierce, Assistant Surgeon General of the United States Public Health Service, described the work being done by his department to educate the people of the United States on the seriousness of the menace from venereal diseases, and he asked for the co-operation of the members of the Conference in this work. After a lengthy discussion, it was unanimously voted to approve the campaign against venereal diseases and that the Conference will co-operate in this campaign in every way that circumstances governing its member colleges will permit.

The report of the Secretary-Treasurer, Dean Theodore J. Bradley, of the Massachusetts College of Pharmacy, showed that there were forty-five member colleges in the Conference. The cash receipts during the year were \$1,126.95 and the expenditures were \$794.63. On April 30, 1920, there was a balance of \$993.59 in the treasury.

Reports of the various standing and special committees were received as follows:

Executive Committee—Henry Kraemer, of Michigan, Chairman.

National Syllabus Committee—T. J. Bradley, of Massachusetts, Chairman.

Standing Committee on Higher Educational Standards—W. J. Teeters, of Iowa, Chairman.

Standing Committee on Faculties—Zada M. Cooper, of Iowa, Chairman.

Standing Committee on Curricula and Teaching Methods—C. B. Jordan, of Indiana, Chairman.

Standing Committee on Activities of Students and Alumni—R. A. Lyman, of Nebraska, Chairman.

Standing Committees on Uniform College Bulletins—C. O. Lee, of Indiana, Chairman.

Standing Committee on Relations of Pharmacy Schools and other Professional Schools—E. F. Kelly, of Maryland, Chairman.

Standing Committee on Examination Questions—E. A. Ruddiman, of Tennessee, Chairman.

Standing Committee on Research—Albert Schneider, of Nebraska, Chairman.

Special Committee to Consider and Report on the Question of

the Establishment of Two Classes of Pharmacists and Corresponding Courses in Colleges of Pharmacy—Jacob Diner, of New York, Chairman.

Special Committee to Work Out Methods of Presenting the Advantages of Pharmacy as a Calling to High School Students—J. A. Koch, of Pittsburgh, Chairman.

Special Committee to Prepare and Distribute Information on Pre-requisite Legislation—W. B. Day, of Illinois, Chairman.

All of these committee reports will be published in the proceedings of the Conference and several of them will appear in other publications.

The West Virginia University Course of Pharmacy was elected to membership in the Conference.

The following officers were elected for the ensuing year:

President, Wilber J. Teeters, of Iowa City, Iowa.

Vice-President, Washington H. Keigler, of Charleston, South Carolina.

Secretary-Treasurer, Theodore J. Bradley, of Boston, Massachusetts.

Chairman of the Executive Committee, Rufus A. Lyman, of Lincoln, Neb.

Members of the Executive Committee—Julius A. Koch, of Pittsburgh, Pennsylvania, and Wortley F. Rudd, of Richmond, Virginia.

Member of the Syllabus Committee, 1920-1927, William C. Anderson, of Brooklyn, New York.

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## BOOK REVIEWS.

LABORATORY MANUAL OF COLLOID CHEMISTRY. By Emil Hatschek. Small 8vo., 131 pages, contents, indexes and twenty illustrations. Philadelphia, P. Blakiston's Son & Co. \$2.00 net.

If we could make the somewhat grotesque supposition that Thomas Graham might return in the flesh, he would be greatly astonished to see how his acorn has grown to a forest. Introducing, as he did, more than half a century ago the terms "colloid" and "crystalloid," and describing many striking and interesting procedures based on the differing properties of the two types of substances, the deeper significance of his researches remained for a long while unknown.



For many years, physicists and chemists were wont to speak of the two types as representing different classes of substances, but we now know that the differences are those of condition and that any substance may assume either state. Colloidal conditions of even the very active elements, such as sodium, can be obtained. It appears, indeed, that some of the phenomena that have been designated as liquid crystals, may be really due to colloid suspension.

The author of this book is so well known in the field to which it is devoted that we may feel sure that it will be of high merit. It is especially so because it deals with a phase of the subject that has not received as much attention as needed, namely, the actual work in preparing and studying colloids. A good deal of the literature has been taken up with the theory and applications, and a book, such as is here presented, which gives practical details of many experiments will be especially welcome to the older chemist whose studies date from time when phenomena were merely given passing notice in the instruction. In fact, as one writer lately said, some of the most important facts in physical chemistry were presented in a highly indirect way. Allotropism was discussed always under ozone, dimorphism under sulphur, colloid state under silicic acid, and catalysis in connection with the production of oxygen from potassium chlorate.

The work has nineteen chapters, each devoted to a special phase of colloid phenomena. The first chapter takes up the general methods of procedure, pointing out the great importance of cleanliness, and the liability of error from the inferiority of the glass used in many of the laboratory vessels. Test-tubes are often found that in a short time will communicate enough alkali to pure water to produce a pink tint with phenolphthalein. Such tubes are quite unfit for use. The difficulty of cleaning vessels after certain experiments is pointed. Thus, while suspensoid sols are generally easily removed, the emulsoid forms are much more difficult. Traces of gelatin or albumin are difficult to remove and very objectionable if not removed. A special chapter is given to the methods of producing the curious rings known as the Liesegang phenomenon. The original method with chromated gelatin and silver nitrate is given and then several other forms, of which those with silicic acid gel will be of special interest to mineralogists, since banded deposits are not infrequently noted in minerals.

The book is a valuable addition to the literature of the subject,

and will be of especial value to those chemists engaged in teaching general chemistry, as it gives methods of performing a large number of interesting and instructive experiments.

- H. L.

TREATISE ON GENERAL AND INDUSTRIAL INORGANIC CHEMISTRY.

By Dr. Ettore Molinari. Second edition, translated from the fourth revised and amplified Italian edition, by Thomas H. Pope, B.Sc., F.I.C., A.C.G.I. 8vo., xix-858 pages and index, 328 illustrations and two phototype plates. Philadelphia, P. Blakiston's Son & Co. \$12.00 net.

This handsome, well printed and well bound volume contains an immense amount of information on a wide range of subjects. It differs from most books within the field, by having a considerable space devoted to the history of chemistry and to the general principles of the science as now taught. In fact, some statements are made in regard to early civilizations, going back to the ancient Egyptian and Babylonian periods. It is doubtful if so extensive a treatment of the history is a profitable use of time and space in a book of this character. So much of our knowledge of the earlier civilizations rests upon scanty data that it is unwise to express positive opinions about them. An examination of Dr. Molinari's statements shows that claims are made for discoveries that are hardly so well established as to form basis for argument as to the development of science in those days. The interpretation of the Confucian philosophy in terms of modern ethics is rather rash.

One hundred and thirteen pages are devoted to an exposition of the principles of modern chemistry, especially the physico-chemical features which bulk so largely now in all text-books and teachings of the science. While even in this field the critic may doubt the wisdom of the introduction of such matter, it can be said that it is well done and the perusal of these pages will be of much use to the beginner in chemistry.

Turning to the main feature of the book, the description of industrial processes in the inorganic field we find a very large amount of interesting and valuable data. The classification is by elements beginning with hydrogen and following with groups mainly in the now fashionable order of the periodic system, but broken here and there on account of special relationships. Thus, the so-called "noble" gases are taken up in connection with nitrogen on account of their regular existence in the atmosphere. In this connection it

is to be noted that the author gets wrong on the helium bibliography (as every one else seems to do) for he says that "N Lockyer" discovered it in the solar chromosphere in 1867. It was in 1868 that J. N. Lockyer saw a line near but not identical with the sodium lines while examining the spectrum of a solar prominence. Reference is made to Palmieri's observation of a peculiar line in the spectrum of material from Vesuvius, but no mention is made of Hillebrand's experiments on cleveite. It is to be regretted that no mention is made of the peculiar application of helium as a substitute for hydrogen in dirigibles and the large amounts of the gas that were obtained in the United States for use in Europe, just prior to the armistice, but doubtless the time has been too short for the incorporation of such details.

It will not be possible in the space available to present in any detail the merits of the book. The amount of information it contains is very large. The translation appears to be well done, and the translator has very wisely made an occasional note when he feels that the author's statement has lost its value by the progress of discovery or he has accidentally erred. An interesting footnote on the effects of forests on rainfall states that on the island of Malta, the replacement of forests by cotton areas has caused the rainfall to be often deficient, while the afforestation of St. Helena has increased the annual rainfall to three times what it was when the "little corporal" was the resident.

Dr. Molinari's book deserves the success it has had for the first edition was soon exhausted, and it constitutes a valuable addition to library of both the teaching and works chemist. H. L.

THE PROFESSION OF CHEMISTRY. By Richard B. Pilcher, Registrar and Secretary of the Institute of Chemistry of Great Britain and Ireland. Constable Hall & Co., Ltd., London, England.

"When a boy turns a room—probably his bedroom—into a laboratory and starts making experiments the results of which are commonly obnoxious to the other members of his home, and when the household is startled by explosions and the smell of sulphuretted hydrogen penetrates to his father's study the question immediately occurs to the parent, 'How can the boy become an analytical chemist?' Afterwards he learns that the adjective *analytical* is too restrictive, but we will deal with that later."

The foregoing quotations from the preface of this book gives an idea of its purpose.

The author, who is a well known English authority, gives a synopsis of the education and training recommended for the profession of chemistry; beginning with preliminary education and leading up to a description of the requirements for admission into that ancient and honorable body known as the Institute of Chemistry, a Fellowship in which is one of the highest honors that can come to a chemist.

The book is divided into the following general headings:

A. *Education and Training:*

1. General education.
2. Matriculation or Preliminary Examination.
3. Technical training.
4. Qualification (including degrees in course).
5. Higher qualification (including post-graduate degrees).

B. *Possible Careers for a Chemist:*

1. Consulting practice.
2. Industrial practice.
  - Analytical.
  - Research.
  - Works control.
  - Consulting technological.
3. Official chemical appointments.
4. Teaching.
- 5 and 6. Combinations of the foregoing.

A very interesting chapter in the early part of the book is concerned with the discussion of the differentiation between pharmacists and chemists, for in England the pharmacists are usually called chemists whether they possess any specialized training along that line or not. The confusion in terms is explained by the author who contributes some interesting historical data in connection therewith.

In the chapter on Professional Training, the following paragraph will find unqualified approval among teachers of chemistry:

"The sciences with which a chemist must be acquainted are to connected and so enlighten one another that it is impossible for him to obtain a competent knowledge of any one branch without an acquaintance with at least the fundamental principles of several allied branches. Though he has comparative mastery over one

science he will find the study of that obscure if he neglects others, and these, though subsidiary, should be pursued to such an extent that the knowledge acquired is real and useful. The man with a smattering is found to be a source of danger in his profession, while he contributes to the crowding out of the more competent. The trained technical man's bag of tools is his brain; the tools consist of the departments of knowledge he is able to exercise; the better he is able to use them by the aid of his 'common sense,' the more successful is he likely to be in practice; the broader his training, the better his equipment."

Under Professional Organizations, the author declares: "Membership should be sought, therefore, from a desire to assist in maintaining the prestige of the profession generally as much as for any direct advantage to the individual."

Much that is of interest and value will be found throughout the book which deserves a careful perusal. The concluding chapters are along constructive lines and are headed: Chemistry and the State, Teaching, Women in Professional Chemistry, and Chemists in War. The book is well indexed and should find a place in every chemist's library.

C. H. L.

FOOD INSPECTION AND ANALYSIS FOR THE USE OF PUBLIC ANALYSTS, HEALTH OFFICERS, SANITARY CHEMISTS AND FOOD ECONOMISTS.  
By Albert E. Leach, S.B. Revised and enlarged by Andrew L. Winton, Ph.D., 4th edition. John Wiley & Sons, Inc. \$8.50.

This valuable work, used both as a working manual and as a reference book by food officials, who usually refer to it simply as "Leach's," is always welcomed in a new edition, for there are so many changes and improvements in methods and so much valuable data is constantly accumulating that a book of this type should be revised at least every five years.

The present new (4th) edition has been increased in size by 90 pages over the previous edition. This in reality means a much greater increase in new matter, for the bibliographical notes at the end of each chapter have been eliminated entirely, as they were by no means complete and were frequently misleading.

Space has also been gained by the discontinuance of a large amount of tabulated matter in Chapter 2 of the 3d edition, on reagents.

A chapter on the hydrogen ion concentration and its determination

by means of electrical apparatus, by Professor Gerald L. Wendt, has been added and constitutes a valuable new feature of the work.

It seems hardly necessary to go into a detailed description of the valuable features of the book, for it has come to be recognized as authoritative in its field and to combine descriptions of analytical methods with comparative data of composition in a comprehensive manner, which has never been attempted in any other work of this kind.

There are some disappointing features in the present revision, however, which should be mentioned, in the hope that the next revision, which should now be in course of preparation, will be free from certain defects that have been carried through from earlier editions, and that some important omissions may be supplied.

On page 968, under Copper in Vegetables, it is stated that "In the Massachusetts market labels like the following are not uncommon: 'This package of French vegetables contains an equivalent of metallic copper, not exceeding three quarters of a grain.'" The foregoing statement certainly has not been true for some years past, nor can the following statement regarding saccharin, on page 969, find support in fact at the present time: "Saccharin is claimed to possess antiseptic powers and is used in canned goods, but its primary purpose is as a sweetener."

The following statement on page 1014 is another instance of careless editing: "Caffein, extract of cola leaves, and cocaine are ingredients of proprietary syrups and beverages." It is news to learn that cola *leaves* are used for this purpose and rather remarkable that no mention is made of the antinarcotic act in connection with cocaine, which has long since disappeared from use in beverages, if indeed, it ever were present in appreciable amounts.

Under Nut Butters the only data given are on two brands common in England but not known in this country and no mention is made of any American brand whatever.

More complete data and a more comprehensive discussion of the subject of vinegars is extremely desirable, especially of glucose and molasses vinegars and in the interpretation of results on apple cider vinegars.

The egg substitute section is by no means up to date. The latest references seem to be to products examined in 1895 and no mention is made of the fifty or more brands which were on the market

as long as four or five years ago, data concerning which are available in numerous official publications, both State and National.

It would be extremely desirable to have a chapter devoted to canned soups, and miscellaneous canned products so abundantly used nowadays. Also more complete figures are desirable in connection with canned vegetables and fruits, in order to properly interpret results, particularly with reference to relative proportions of liquids and solids.

Although the vitamins are not capable of even approximate analytical determination at the present time in a practical way, it is surprising that this new and important group of food accessories is not even mentioned.

Notwithstanding these few drawbacks, the book is one which is indispensable to the practicing food analyst or food expert and should be in every reference library as well.

C. H. LAW.

FOOD POISONING AND FOOD INFECTIONS. By William G. Savage.

This recently issued volume of the valuable list of scientific publications, issued under the name of the "Cambridge Public Health Series," is both timely and important. It contains 241 pages and is well indexed. Food poisoning in the popular mind and to a certain extent even among physicians and chemists, has been a curious jumble of fact and fallacy in which the newspapers have made bad matters worse by their unintelligent use of such terms as "ptomaine" and the encouragement of the belief that it is the metallic substances present that usually cause the unfavorable symptoms sometimes attributed to tinned foods.

The chapter headings which give one an intelligent idea of the value and comprehensiveness of the book are as follows:

1. Introductory and historical;
- 2, food as a vehicle for transmitting bacterial diseases;
- 3, foods inherently poisonous;
- 4, food idiosyncrasy;
- 5, the clinical and general features of outbreaks of food poisoning;
- 6, the Gaertner group of bacteria in relation to food poisoning;
- 7, food poisoning of unspecific bacterial origin;
- 8, certain special kinds of food poisoning;
- 9, botulism;
- 10, sources and methods of infection in food poisoning outbreaks;
- 11, chemical poisons in food, unintentionally introduced;
- 12, chemical poisons deliberately added to food;
- 13, the prevention of food poisoning outbreaks;
- 14, methods of investigation of food poisoning outbreaks.

Bibliographic references are freely given. It is strange that no

mention is made, among the poisonous plants enumerated, of the oxalic acid containing sorrel and rhubarb leaves which several times within the past few years have been alleged to have caused serious toxic effects when eaten.

In the chapter on chemical preservatives frequent references are made to the U. S. Food and Drugs Act and the decisions of the Referee Board, and the author criticizes the policy of inaction which has hitherto guided the British authorities upon the subject and makes a number of suggestions which are of constructive value.

The book is one which should be in every medical and chemical reference library and will be found useful as well by health officials who are frequently confronted with puzzling cases of alleged food poisoning.

CHARLES H. LAWALL.

A CRITICAL REVISION OF THE GENUS *EUCALYPTUS*. By J. H. Maiden, I.S.O., F.R.S., F.L.S. (Government Botanist of New South Wales and Director of the Botanic Gardens, Sydney). Vol. IV. Parts 9 and 10.

These two parts constitute Parts XXXIX and XL of the complete work of this important classic monograph. These continue the same style and presentation of the subject matter as the preceding parts. Part XXXIX is the treatise on the following species of *Eucalyptus*: *E. Torelliana* F.v.M.; *E. corymbosa* Smith; *E. intermedia* R. T. Baker; *E. patellaris* F.v.M.; *E. celastroides* Turczaninow; *E. gracilis* F.v.M.; *E. transcontinentalis* Maiden; *E. longicornis* F.v.M.; *E. oleosa* F.v.M.; *E. Flocktoniæ* Maiden; *E. virgata* Sieber; *E. oreades* R. T. Baker; *E. obtusiflora* DC; *E. fraxinoides* Deane and Maiden.

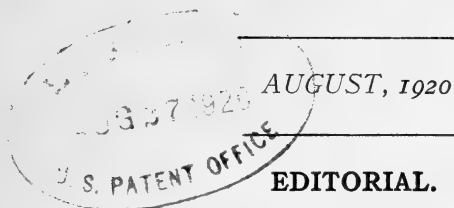
Part XL considers the following species: *E. terminalis* F.v.M.; *E. dichromophloia* F.v.M.; *E. pyrophora* Benth; *E. lævopinea* R. T. Baker; *E. ligustrina* DC; *E. stricta* Sieber; *E. grandis* (Hill) Maiden.

The artistic illustrations that have been so characteristic of these monographs are likewise continued in the parts now before us. The data associated with the descriptions are of material commercial value, as well as botanical monographs of the highest type.

G. M. B.



# THE AMERICAN JOURNAL OF PHARMACY



EDITORIAL.

## ENGLISH ORTHOGRAPHY.

Orthography, the topic selected for editorial comment this month, is defined by lexicographers as the art of writing words with the proper letters according to accepted usage: the part of grammar which treats of the nature and properties of the letters and of the art of writing words correctly. It is derived from the Greek *orthos*, right, straight, correct, and *grapho*, I write. In other words, it is *correct spelling*, and to spell "is to write or print words with their proper letters." An orthographist is one who *spells correctly* or in accordance with the rules of grammar. It would be interesting, if it were possible of determination, to learn what percentage of Americans at this time could lay claims to such a designation. Likewise, to ascertain the relative influence of perverted educational methods and of passing literary styles in causing the lamentable lack of knowledge of this part of grammar exhibited by such a large proportion of the present generation.

This subject has received but scant consideration in pharmaceutical literature, possibly because pharmaceutical journalism, very happily, has not, to any appreciable extent, been influenced by the propaganda for spelling reform. The article entitled "The End of Simplified Spelling" from the *Montreal Pharmaceutical Journal*, reprinted in this number of the JOURNAL, is commended for careful perusal. In our correspondence and intercourse with pharmacists we have noted that comparatively few have been carried away by this fad and, moreover, that some of these have rather lately joined in the fag end of the movement.

The medical and chemical journals of America have declined to adopt the more radical changes in spelling that have been advocated. The principal modifications that some of these have adopted have been the substituting of "f" for "ph" in such words as sulphur and in dropping the silent "e" in words ending in "ide," "ine," etc. These modifications are not uniformly carried out in these scientific journals nor are they universally approved of or followed by the members of the scientific and professional organizations representing these vocations. The same may be said of the journals covering the other technical, scientific and professional fields.

The conservative spirit actuating the medical, pharmaceutical and chemical professions and the adherence of the representatives of these to the established rules of spelling was shown by an incident that occurred at the Decennial Pharmacopoeial Convention held in Washington in May. The word "pharmacopoeia" is admittedly a difficult word to spell and has been at times misspelled even in official literature relating to the pharmacopoeial conventions. Yet when a motion was offered to drop the second "o" in the spelling of the word "pharmacopoeia" it was howled down and the preponderance of sentiment against dropping this silent "o" was quite in evidence.

It is doubtful if very many of the followers of these so-called "reforms in spelling" have given any real serious thought to the portent and the influence that the success of the changes advocated might possibly have upon our language or even upon the nation itself.

Roget has stated some of the important functions of language in the following pertinent abstracts:

"The writer, as well as the orator, employs for the accomplishment of his purpose the instrumentality of words; it is in words that he clothes his thought; it is by means of words that he depicts his feelings \* \* \* \* Words are the instrumentalities by which we form all our abstractions, by which we fashion and embody our ideas, and by which we are enabled to glide along a series of premises and conclusions with a rapidity so great as to leave in the memory no trace of the successive steps of the process; and we remain unconscious of how much we owe to this potent auxiliary of the reasoning faculty. \* \* \* \*"

"It is of the utmost consequence that strict accuracy should regulate our use of language, and that every one should acquire the power and the habit of expressing his thoughts with perspicuity

and correctness. Few, indeed, can appreciate the real extent and importance of that influence which language has always exercised on human affairs, or can be aware how often these are determined by causes much slighter than are apparent to a superficial observer."

The history of the English language is a very interesting study. It has gone through several stages of development and Modern English, the cultivated language forming our Standard English of today, is declared by competent authorities to be so distinctly different from Old English or Anglo Saxon as to constitute these, for all practical ends, two distinct languages as much so as Latin and Spanish. It is a mixed or polyglot tongue exhibiting in its extensive vocabulary the modifying influences of invasion, conquest, wars, explorations, expositions, commerce, advances in the professions, arts, sciences and industries, and the progress of literature throughout the centuries. Intercourse with other nations has added many words from the French, German, Portuguese, Italian, Dutch and other languages.

Nevertheless, the root words have been generally retained intact and the newer words formed therefrom have followed the spelling of their predecessors and the established rules. The forms of pure words have come down to us from the past generations. Of the great body of words constituting the English language the spelling is determined by established usage and the rules of grammar that proclaim such usages are the laws of that science. The spelling of a language is really a process of sifting out and it is the special province of lexicographers to determine the correct spelling in accordance with the principles enunciated in these laws and their conclusions embodied in the accepted dictionaries become the authority or standard of good English, alike for spelling, pronunciation and meaning.

The natural changes that take place in the language are due to many and varied causes whose influences effect gradual innovations recognized by usage and reflected in the dictionaries. Among such may be cited, as examples, labor instead of labour, physic for physick, toils for toyls, choose for chuse, virtue for vertue. Many similar changes have been and are continually going on, almost unperceived, as a part of the process of language evolution and without violating the sense of propriety or infracting the rules of our orthography. We conceive it to be the duty of all English-speaking peoples to preserve the purity of our language.

Reformation is an act of changing from worse to better and not from bad to worse. Such reformation of our language as takes place should be by the orderly processes of *evolution* directed through the proper channels and not by *revolution*. Evolution and not revolution is the line of true progress and staid reform.

We do not assert that there are not some words in the English vocabulary for which simplified spelling would be justified. We are, however, of the opinion that the innovations urged by the enthusiastic propagandists for simplified spelling were entirely too radical and revolutionary and would have upset long established rules and many good authorities. Further, it is our belief that many who joined in this movement had no conception of the basic principles of our orthography and some were purely faddists, while others with insincerity sought a cloak for their own imperfect knowledge and offered as a subterfuge "simplified spelling" that made their already incorrect spelling simply abominable and excused as "phonetic" much that had passed from the state of being funny to the absolutely ridiculous. Whatever claims the movement may have possessed for recognition as a scientific proposition were thus discounted and drowned out by the preponderance of the unscientific exhibitions and it is probable that its actual effect upon English orthography will be quite limited.

By common consent literateurs have been granted privileges with the languages for the purpose of enhancing the art of their profession and, for the sake of rhyme or meter, the poet at times exercises the "poetic license" to modify or to curtail the spelling of a word. This, however, is expected to be done in accordance with literary art and in a constructive manner. At no time, however, has it been conceded that the newspaper or magazine writer, the occasional contributor, the novice or the irresponsible student was privileged *ad libitum* to change the accepted and authorized spelling of English words. Such a procedure would be destructive of the very foundation principles of the language. The ever-widening breaches and the increasing number of words whose spelling was being erratically "simplified" showed the danger to our language from such promiscuous and unauthorized changes.

Editors, as a rule, are not easy prey to false ideas or fads, and it is to their credit that the great majority of American editors have adhered firmly to the authorized and accepted spelling of the dictionaries. Some have adopted the minor and more conservative

modifications proposed, such as "thru," "thoro" and "tho." A few phave not only advocated and used in their publications the simplified and phonetic spelling proposed for common words, but have assumed the authority to add other changes in support of erratic personally made rules.

A rule of grammar that was firmly impressed upon the mind of the writer in his school-days reads "A Regular Verb is one that forms its Past Tense and Perfect Participle by the addition of ed to its present tense." Doubtless, the same rule is still extant in English grammars. In one of our magazines we note the continuous use of such words as "accomplisht," "warpt," "helpt," "suckt," "increast," "rankt," "publisht," "distinguisht," "discust," "focust," "talkt," "decreast," "kilt," etc. Every one of these quoted words are regular verbs and every such deliberate infraction of grammatical rules becomes a mutilation of standard English.

It must be viewed as an unjustifiable assumption that the Editor's knowledge and authority is superior to that of grammarians and lexicographers. It may be construed as a lamentable exhibition of affectation or of self-satisfaction mistaken for editorial service. No one will object to good English or take exception to the use of accepted and authoritative spelling, and it does not appear to the writer as coming within editorial propriety and good taste for an editor to offend continuously by such atrocities a large portion of his readers whose education, love and loyalty thereto, cause them to adhere closely to the standards for purity of our language. It is not the province of an editor to destroy the Nation's language or to take uncalled-for liberties therewith any more than he could with the property of the Nation.

We cannot believe that such pedantry is helpful to the promiscuous class of readers of a magazine. Imagine a reader in South America or in France trying to read the article referred to in which "kilt" appeared; he turns to his English dictionary for the meaning of the word "kilt" and learns that "kilt, is to truss or gather one's clothes in a bunch; a kind of short petticoat worn by men in the Highlands of Scotland" instead of the past tense of kill, as was here intended. Our conception of an editor's duties leads us to believe that he should have a due regard for the feelings of his readers.

The attitude of the Editor referred to is comparable to the anecdote of Nancy who was saying her prayers. "And please God," she petitioned, "make Boston the capital of Vermont."

"Why Nancy," exclaimed her mother, "what made you say that?"  
"'Cause I made it that way in my examination."

The AMERICAN JOURNAL OF PHARMACY, under the present editorial management, will adhere closely to the rules of spelling warranted by usage and accepted authorities. Our exceptions to the spelling of the standard dictionaries will be only those which have been adopted in the United States Pharmacopoeia, as, for example, the distinction of alkaloids by the termination "ine" and the retention of "in" as the terminating letters for neutral principles. The Pharmacopoeia has adopted in only a few instances a distinct form of spelling for a limited number of articles for the sole purpose of avoiding error in either distinguishing the article or in its administration. We consider it incumbent upon medical and pharmaceutical journals in the spelling of these words to follow these pharmacopoeial modifications. These are, fortunately, from a philological view point, only minor changes that do not seriously infract the established rules of English orthography. G. M. B.

#### DENATURING OF BAY RUM.

In Regulations No. 60, the Bureau of Internal Revenue provided for denaturing of bay rum by the addition of not less than one-fourth grain of tartar emetic to each fluidounce.

Objections have been offered to the use of such a toxic substance as an antimony salt for this purpose and the Department has since issued several memorandums modifying this provision and permitting the use of other denaturing agents. These are not less than five grains of resorcin, or two grains of quinine sulphate, or two grains of cinchonidine sulphate, or five grains of salicylic acid, or five grains of sodium salicylate per fluidounce.

It would appear that these modifications have been proposed largely in the interest of certain manufacturers of hair preparations and toilet articles in which such modifying agents were used in the formulas of the preparations manufactured. These denaturants have not been considered as yielding a product that is satisfactory for the general sale of bay rum in the trade as a toilet water.

A recent decision of Prohibition Commissioner Kramer adds to the list of permissible denaturants for bay rum the addition of the soluble matter of not less than two grains of the pulp of the Colocynth fruit (*Citrullus Colocynthis*) to each fluidounce of the preparation.

In our opinion this will prove a more desirable denaturant for bay rum and other toilet waters and the medication will be sufficient to deter the use of such products as beverages.

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## THE BIOLOGIC METHODS FOR DIGITALIS ASSAY.\*

BY HERBERT C. HAMILTON.

DETROIT, MICH.

There are many steps in the process of transforming the lovely old-fashioned flowering plant, fox-glove, into the powerful medicinal product known as the digitalis heart tonic. In fact, some of the steps might be called stopping places and regarded as of more than passing interest; especially such points as the selection of some one out of the many varieties of digitalis to be the official one, the choice of the portion of the plant to be used, the age of the plant, and the menstruum for extraction. The seriousness of these problems may be judged by the last mentioned, since the U. S. P. Revision Committees have, on each occasion, selected a different menstruum for extracting the crude drug.

But of all the problems demanding attention, probably no one has received more than that of proper means of testing and standardizing the crude drug and its extracts. From the time of Fagge and Stevenson's work<sup>1</sup> recorded in 1866 up to the present time, the controversy has raged unceasingly.

These investigators first used the method later modified and known as the Focke method<sup>2</sup> by which the frog was injected in the thigh, the heart exposed and the time noted when the heart stopped in systole.

Koppe, in 1875,<sup>3</sup> studied the action on warm-blooded animals, noting the effect on the heart but especially the amount necessary to induce vomiting. This was later suggested by Hatcher<sup>4</sup> as a means of standardization.

Bennefeld,<sup>5</sup> in 1881, in his careful examination of tinctures of digitalis from different parts of Germany, selected the method later known as the Hatcher Cat Method,<sup>6</sup> the diluted preparation being slowly injected into the vein of a rabbit until death occurred.

Bardet,<sup>7</sup> in 1889, used the frog in the way later suggested by Houghton, that is, comparing activities on the basis of the minimum lethal dose.

Houghton,<sup>8</sup> in 1898, first published the method and described the exact technic by which to standardize the digitalis preparations. The method, at time of publication, had actually been in practice for three years and is the first recorded attempt not merely

\*Paper read at the St. Louis meeting of the A. C. S. and published by courtesy of the American Chemical Society.

to test but really to establish uniformity in preparations of this drug.

Prevost,<sup>9</sup> in 1893, used frogs and chose as end-point the systolic stoppage of the heart.

Fraenkel,<sup>10</sup> in 1902, was the first to apply this method, now official in the U. S. P.,<sup>11</sup> as an exact method for quantitative assay, selecting one hour as the time for systolic stoppage.

Focke,<sup>2</sup> in 1902, and frequently at later dates, wrote on the use of frogs for standardizing digitalis. He selected the systolic stoppage in 7 to 10 minutes as the end-point and suggested a formula by which to deduce the value from the data, including the weight of the frog, the dose and the time of systolic stoppage. He has written voluminously on the subject.

From this time on no absolutely new method has been devised, the research being confined to modifications and adaptations of the methods proposed by earlier workers.

Such is the Hatcher Cat Method,<sup>6</sup> the Reed and Vanderkleed Guinea Pig Method,<sup>12</sup> the M. S. D. Frog Heart Method,<sup>11</sup> and the Pittenger Gold Fish Method,<sup>13</sup> although the latter is the only published one using this test object.

Laying aside for the moment the question as to the validity of any of these methods, we should attempt to consider, in a broad way, the more or less derisive question, "Is the sample of drug that has been found to possess the greatest power to kill a cat, the one that will prove most efficient in curing a man?" Rusby<sup>14</sup> is skeptical of such methods because as a botanist he is not fully informed as to their applicability.

Lloyd,<sup>15</sup> perhaps for the same reason, says in reference to a toxicity experiment recorded by Withering: "In those days of heroic medication it was naturally concluded that a drug that could thus kill a turkey must be good medicine to cure a human being, a process of reasoning not yet altogether obsolete."

Beal,<sup>16</sup> with no circumlocution but directly to the point, says: "If we would know the physiologic action of a drug upon the human we must observe its action on the human, this cannot be deduced with any degree of certainty by its action on one of the lower animals."

All these comments are based on a wrong conception of pharmacology. While there are occasional instances where the action of a drug on one animal differs fundamentally from that on another or on a human, such anomalies are usually traceable to fundamental differences in the two species. To illustrate, the cat and dog vomit



easily, the guinea pig not at all. The frog will not respond to the action of a febrifuge since its temperature is always that of the surrounding medium. But all, including man, have the heart and the circulatory system which either directly or through the nerves are acted upon by external influences such as drugs. Certain features of these effects may differ, but fundamentally the fact remains unassailable.

We therefore take issue with Beal to this extent, that while there are unquestionably cases in which the action of a drug on man differs materially from that on certain animals, these are exceptional cases.

Practically every physiological reaction in man has its counterpart in some animal.

It is on this basis that the science of pharmacology is founded. Through the investigation of the action of drugs on animals many of their valuable properties have been discovered; by this means most of these actions have been explained. Digitalis acts as a diuretic. Is it a direct action on the kidneys or is it only an indirect effect of its action on the circulatory system? By animal experiment and not by observation of humans this has been made clear. Digitalis has a strongly tonic action on the heart and vessels. Is its action directly on the muscles or is this an effect of its action on the nerves? Again we are rewarded by the answer as a result of animal experiments.

But the critic is perhaps still dissatisfied. Granted that all this is true he yet is skeptical on one or two points. How is it possible to standardize drugs even if the action on some animal is apparently similar to its action on man? This is a logical question and deserves an answer.

Digitalis administered to animals in doses comparable to the therapeutic dose for man does not show a measurable effect except when such doses are given intravenously to an anesthetized animal, the effect being measured by the aid of a myocardiograph or similar instrument—a measurable effect sufficient for qualitative purposes. For a quantitative test comparison must be made with a standard just as the chemist must have absolutely pure reagents or must be able to discount the impurities by running a blank or some similar procedure.

Digitalis will slow the beat of the heart, increase the amplitude of the beat, raise the blood pressure, but the amount necessary to bring about a definite degree of change in these measurable reactions differs with different dogs, so the effect of the sample on one dog cannot be compared with the effect of the standard on another

dog. By use of a number of dogs an average could be selected, but time and the expense of labor and animals will not permit this procedure. Again, to compare sample and standard on the same animal by means of consecutive injections is not practicable because the elimination of digitalis is so slow that the animal never fully returns to its original condition to permit comparing two injections even of the same sample.

For these reasons, attempts to use this as the end-point have been abandoned and the death of the animal or in the case of frogs, stoppage of the heart in systole selected.

Not only, therefore, can the action of drugs on the human be deduced from that on the lower animals, but also the degree of the action can be measured and the exact manner of action explained.

Lloyd's statement in reference to killing a turkey and curing a man may have been true in those days when the science was undeveloped. At present, however, the fact of killing is of little importance; the vital points in the experiment are the amount that killed, the action of smaller doses and the possibility of applying the substance clinically to relieve a pathological condition.

There is no known medicinal substance which, taken in excessive quantities, does not induce toxic symptoms and in most cases, death. It is not valuable because of this but in spite of it.

The question raised by Rusby is entirely logical and *apropos*. If a substance is standardized solely on the basis of its M. L. D. with no regard to the characteristic effect which that substance may be expected to produce, common sense suggests that such a test is inadequate and should be used only if no verifying effect is available. We will attempt to apply this test of adaptability to the various methods for the assay of the digitalis series, disregarding the question of accuracy and keep in mind only whether the test shows digitalis glucosides and no other poison to be present.

The Gold Fish Method, while little known or practiced, is a proposed means of assaying digitalis by its toxic action on gold fish, the drug being mixed in various dilutions with the water in which they swim. The end-point is the dilution which kills after a certain period of contact and with due regard to certain factors, such as the temperature of the medium. It has the advantage of being one of the simplest and probably cheapest of all. But for the fact that there is nothing typical of digitalis in the action of the drug on the test animal there is no reason why it should not have a

favorable consideration. The gold fish, however, is exceedingly sensitive to substances not always recognized as poisons and certainly not in the same class with digitalis. While the chances of a foreign and more toxic substance being found with digitalis are remote, they are always possibly present as every manufacturer knows. Without a confirmatory test, the gold fish M. L. D. method is to be classed as questionable.

The guinea pig method is no less open to question on the same score, although the results obtainable purely on toxicity are quite uniform and accurate. In this instance, also, there is no observable reaction characteristic of digitalis either before or after death; and death often results from respiratory paralysis rather than a direct action of digitalis on the heart.

The method is simple and as described by the authors inexpensive, since the intention is to use guinea pigs already used for another purpose for which they no longer are eligible, and therefore with a value theoretically nil.

Injection is made subcutaneously and results recorded after a definite period. Results show that pigs, while fairly uniform, have individual variations as well as seasonal, but these can be eliminated as factors in the assay, by the occasional test of the standard and by the use of a number of pigs to obtain the average M. L. D.

The Hatcher Cat Method seems to have even less to recommend it since there is nothing characteristic of digitalis in the death of the animal and further its inaccuracies have been the subject of comment by several authors. Hatcher<sup>6</sup> noted that in some cases, cats required a dose of 50 per cent larger than the average M. L. D. Robinson and Wilson<sup>17</sup> found in a series of ten cats that the M. L. D. ranged from 70 to 210 per cent. of the average M. L. D. Eckler<sup>18</sup> found a variation of over 100 per cent. in the M. L. D. of cats.

The details first published by Hatcher for the assay of digitalis required that the immediate cause of death should be ouabain, only a part of the M. L. D. was to be brought about by the digitalis. The cat is partly anesthetized in order to open a vein into which is inserted a glass canula. Through this the injection is made slowly over a stated period. The animal must die in less than 90 minutes. The method has been modified by most investigators, especially by those who found any valuable feature in it.

The only radical change, however, is that made use of by Newcomb of the Pharmacy Department of the University of Minnesota.

It is commonly assumed that Newcomb uses the Hatcher Method without material change from that first published, and this opinion will perhaps prevail until some published account of his work appears. Unofficially, however, certain statements have been made such as these: "Hatcher's method, without modification, is of little value." "The cat is the least important part of the method." "The important part of the method is the observation of the action of digitalis on the bundle of His."

One may assume, therefore, that Newcomb discredits Hatcher's Method in which the death of the cat is the deciding factor and pins his faith on observing the heart block which follows fatigue of the auriculo-ventricular bundle. This is, to a limited extent, characteristic of digitalis poisoning and so may be regarded as a valuable feature to distinguish the *character* of the poisoning, but it adds nothing to the accuracy of the only quantitative features which the test possesses, namely, the M. L. D. (minimum lethal dose).

As a qualitative test this feature is admirable; but no pharmacologist has succeeded in making the test an accurate quantitative one unless as yet unpublished.

The M. S. D. Frog-heart Method—the Pharmacopoeial method—is, in brief, to inject the diluted preparation into the abdominal lymph sac of the frog, injecting them in series of three and at the end of one hour exposing the heart to observe its condition. The end-point is, that at the end of the one-hour period, the heart must be stopped in systole while the next smaller dose—a difference not to exceed 10 per cent.—leaves the heart beating at that time. This method has two advantages over those employing mammals, namely, that a sufficient number of test animals can be used to detect and exclude those more or less resistant than the average and to test the standard on a number of similar animals under exactly the same conditions of weight, age, temperature and season, all of which may be variants. It has the further advantage that the end-point can be recognized as being due to one of the digitalis series and to no other poison by the position of the heart in systole.

It has the advantage over Newcomb's modification of Hatcher's method in the greater accuracy in the end-point by having a large number of test animals from which to exclude those of exceptional resistance—either high or low.

The M. L. D.<sup>19</sup> Frog-heart Method has for its end-point the minimum lethal dose—the smallest dose causing death with heart in systole.

The frogs are injected in the abdominal lymph sac with dilutions of the preparation, using such dilutions as to make a total dose less than 1 Cc. The frogs consistently dying with this dose are examined to observe the position of the heart which must be in systole, the same as by the one-hour method.

This has all the merits of the U. S. P. Method with the added advantage that in case of slow absorption the longer time limit permits, in most cases, total absorption. A further advantage lies in the fact that the frogs are not handled roughly, as in pithing and laying bare the heart, a procedure which may tend to influence the results adversely.

A third advantage is in the certainty of the end-point—death—as against the frequent occurrence of a heart at the end of the one-hour period not being positively stopped in systole.

Dr. Edmunds, of the Department of Pharmacology of the University of Michigan, and Dr. Worth Hale, Assistant Dean of the College of Medicine of Harvard University, were called to Washington to carry out such experiments as would determine, if possible, which of the methods is most practicable and reliable for the assay of digitalis. Their results and conclusions appear in *Hygienic Laboratory Bulletin No. 48*.<sup>20</sup>

Regarding Focke's Method, which is used mostly in Germany, they say: "However even with these precautions we believe that this method allows of greater variations and inaccuracies than any other method we employed."

Attempts to apply a test by which the increase in blood pressure is used as the measurable reaction led to the following conclusion: "The blood pressure method upon cats and dogs commends itself on account of the close relation it sustains to the use of the drug in clinical practice. The objections consist in the difficulty of procuring these animals at times, and also the necessity of carrying out repeated tests to confirm the results which a study of our tables show will vary greatly."

As regards the M. L. D. and M. S. D. Frog Heart Methods, they found it impossible to choose with any degree of accuracy. "Between these two methods as far as can be judged in the light of our present knowledge it is largely a question of personal preference or convenience."

Cushny<sup>21</sup> ("Pharmacology and Therapeutics") comparing the action of digitalis on frogs and mammals, says: "The effects

of digitalis on mammalian heart therefore resemble in general those observed in the frog's. The contraction is not prolonged, however, as in the latter and the inhibitory mechanism plays a more important rôle. . . . The heart in mammals is generally found in a condition of diastole in cases of fatal poisoning and this has been supposed to indicate a fundamental difference in the action of digitalis on the amphibian and the mammalian heart. The dilatation is not, however, a direct result of the digitalis but is probably induced by the poisons formed in the heart by its own activity."

It is evident, therefore, that the frog shows a typical effect of digitalis just as distinctly as the mammal, that it can be used in numbers economically impossible in comparison with cats or dogs and thus overcome the factor of individual variations that the digitalis action differs in no material respect from that on mammals.

The very fact that the science of Pharmacology has made such wondrous strides is evidence that the action of drugs on the human may be deduced from that on the lower animals.

The very fact that a system of dosage has been worked out for the powerful drugs shows that their action is measurable by the effects produced.

Few, however, seriously claim to be able to deduce human dosage of a new drug from its effects on experimental animals, except in the most superficial way, and with our present knowledge any such attempt will probably lead to failure.

It is, on the other hand, common laboratory experience to obtain practical working information in regard to a new drug by comparing the intensity of its effects with that of a similar known drug. If, for example, a special preparation of digitalis such as an active principle is produced, its good and bad properties can readily be deduced for human medication by comparing it with *Tr. Digitalis* on laboratory animals.

Or an entirely new local anesthetic can be compared with cocaine on animals and thus obtain actual data as to its effectiveness under most conditions and its comparative toxicity, absorbability and rate of elimination.

Pharmacology is the study of the action of drugs on the lower animals by which much can be learned as to the adaptability of drugs in therapy and their mode of action, their advantages and disadvantages in comparison with others of similar character.

Pharmacological assaying is the application of this information

so that powerful drugs can be standardized although possessing no chemical reactions by which their values can be determined.

The scope of each is distinctly defined, the assay process being subordinate to and based entirely on the pharmacology of the drug in question.

The criticisms of the biologic assay process in general are really without material basis since it is strictly analogous to the chemical assay. Neither assay method attempts to encroach on the clinical application of a drug but concerns itself only with the potency. Both make use of the reaction which most accurately determines the amount of active agent present by use in the one case of chemical reagents, in the other of the animal least subject to variations.

Digitalis, therefore, as one of the most valuable drugs at the command of the physician, cannot be permitted to pass without standardization.

The selection of the method should be based on the most typical effect which is measurable and which is subject to the least variation that is beyond the control of the operator.

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RESEARCH LABORATORY,  
PARKE, DAVIS & COMPANY,  
DETROIT, MICH.

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STUDIES ON COMMERCIAL VARIETIES OF *NUX VOMICA*.

BY H. W. YOUNGKEN, PH.D., AND C. F. SLOTTER, B.Sc.

PHILADELPHIA, PA.

It is thought that *Nux Vomica* was introduced into medicine by the Arabians, but the records in their writings which have been supposed to refer to it are far from clear and satisfactory. Neither is there evidence that the drug was used in India. But it was certainly made known in Germany during the sixteenth century, for Valerius Cordus<sup>1</sup> wrote a remarkably accurate description of *Nux Vomica* about the year 1540. However, it was not until 1770 that it came into use as an article of medicinal value. That value has since increased, owing to the discoveries of Pelletier and Caventou, who isolated the alkaloids, strychnine and brucine, first in *Strychnos Ignatii* and later in *S. Nux-Vomica*, until to-day we find the drug an article of considerable importance.

The seeds are yielded by *Strychnos Nux-Vomica* (fam. *Loganiaceae*), a small tree growing wild in the forest of India, from the eastern seaboard far into the interior, and also in the forests of Ceylon, Burmah, Siam, Cochin China and northern Australia. According to Zörnig<sup>2</sup> and Flückiger<sup>3</sup> they are collected and dried and sent into the market through Bombay, Cochin, Madras, and Calcutta, and thence to London. However, Calcutta is merely a collecting and grading center and does not furnish any distinctive variety of *Nux Vomica*, since there are no trees of that kind anywhere near Calcutta.

The problem, then, confronting us was to determine some means of distinguishing between the present true varieties of the drug. Consequently the Tellicherry, Madras, Cochin, and Ceylon varieties were examined as to the macroscopic and microscopic characteristics. Owing to the small amount of authentic material obtainable for consideration, it is our purpose to present at some later date a continuation of these studies.

The macroscopic examination included a consideration of the following physical characteristics: outline and shape, prominence of the ridge, hilum and micropyle, color and appearance, thickness, diameter and specific gravity. The specific gravity was determined by selecting two representative seeds for each variety, noting their weight in air and loss of weight in water.



# CEYLON NUX VOMICA.

This variety is orbicular and in many cases decidedly concavo-convex. The hilum is prominent and often *raised* (wart-like) with one or two concentric elevations between it and the margin; the ridge is distinct and micropyle prominent. It is either silver-yellow or silver-green in color and vividly glossy, presenting a satin-like appearance; 4 to 7 mm. thick and 15 to 25 mm. in diameter. The specific gravity determined was 1.2102.

# TELLICHERRY NUX VOMICA.

This is orbicular and nearly flat, with the hilum, ridge, and micropyle all rather indistinct and the margin usually acute. It is silver-yellow in color but not as glossy as the Ceylon variety; 3 to 5 mm. thick and 20 to 25 mm. in diameter. Its specific gravity as determined was 1.3521.

# MADRAS NUX VOMICA.

The Madras is nearly flat, orbicular, and shows a hilum not as pronounced as Ceylon, but with the ridge and micropyle prominent. Its margin is usually rounded, the color a dull ash-green, thickness 3 to 5 mm., diameter 15 to 20 mm., and the specific gravity 1.3024.

# COCHIN NUX VOMICA.

Samples from four different sources were examined. They possessed the usual orbicular form, were slightly concave, showed an indistinct ridge, a rather prominent hilum and micropyle and usually a rounded margin. The color was uniformly of a dull silver-gray except in the case of an unwashed sample which was a dull dirty-gray having adhering brownish black patches. The seeds ranged from 4 to 5 mm. in thickness, from 15 to 30 mm. in diameter and gave specific gravities as follows:

(1)	1.2433
(2)	1.3236
(3)	1.2857
(4)	1.3334

For microscopic study, transverse sections were made through the center of the seeds and mounted in chlor-zinc-iodine. They were compared as to the measurements of the outer layer of endosperm cells, the thickness of their walls, length of hairs and the appearance when viewed under polarized light.

Entire hairs ranged in length from  $770$  to  $1300\mu$  in the case of Ceylon Nux Vomica,  $630$  to  $980\mu$  in the Tellicherry,  $630$  to  $700\mu$  in the Madras, and  $630$  to  $980\mu$  in the Cochin variety. The longest hairs were noted on the Ceylon Nux Vomica, but the other observances demonstrated little in the way of diagnostic differences. When viewed under polarized light the hairs of all varieties presented the same striking appearance. Measurements determined for the outer endosperm cells averaged as follows:

Ceylon	$20$ to $31\mu \times 12$ to $15\mu$
Tellicherry	$38$ to $42\mu \times 9\mu$
Madras	$28$ to $31\mu \times 9$ to $12\mu$
Cochin	$28\mu \times 9\mu$

These cells appeared more regularly rectangular in the Tellicherry than in the other varieties.

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### MAKING USE OF NATIONAL AND STATE BULLETINS UPON SCIENTIFIC SUBJECTS.\*

BY CHARLES H. LAWALL, PH.M.

"Know your opportunity," said Pittacus, one of the seven wise men of ancient Greece.

One of the usually unrecognized opportunities of acquiring information and of accumulating a valuable collection of reference pamphlets is that afforded by the publications of the Scientific Bureaus of both State and Nation.

Many of the inquiries which come to the pharmacist from his patrons are upon subjects which are not directly related to his profession, at least not so closely as to be found in any of the textbooks or works of reference that may be upon his bookshelf, and yet closely enough to make him the one logical person in a community to whom such inquiries should be addressed.

\* Read before the meeting of the Pennsylvania Pharmaceutical Association, Harrisburg, June, 1920.

A person who sits on a freshly painted park bench, or who spills gravy somewhere between his Tropic of Capricorn and his Equator, usually rushes frantically to the nearest pharmacist for assistance and relief. How to remove mildew, fruit stains or spots of unknown origin are frequent subjects of inquiry, and it is a wise adviser who will first fortify his knowledge by consulting some authority upon the subject, rather than risk giving off hand and incorrect advice which may result in the ruining of the fabric and the adviser's reputation simultaneously.

It is not generally known to pharmacists, I believe, that a valuable government publication is available, giving information upon these important matters.

It is entitled "Removal of Stains from Clothing and other Textiles," by Harold L. Lang and Anna H. Whittelsey, and is known as Farmers Bulletin No. 861, of the United States Department of Agriculture. This bulletin of thirty-five pages, contained trustworthy information based upon scientific knowledge, for the removal of more than fifty different kinds of stains and spots, and contains complete details for the intelligent use of such solvents, reagents and bleaches as are referred to as being of value. It also contains a complete index. This, unless the supply is exhausted, and any other of the U. S. Government publications, may be obtained upon application to the "Superintendent of Documents, Washington, D. C." For some a nominal fee of five or ten cents is charged, but for many publications, especially those called "Farmers Bulletins," no fee whatever is charged. In writing for government publications much time may be saved by enclosing a small sum in probable excess of the cost of the bulletin if the cost is not known. Enclosures must not be made of postage stamps in payment of fees for government publications, for the government departments, all having the franking privilege, have no use for stamps and are not permitted to take them, so actual currency must be sent.

Another very valuable publication which will be frequently used by those who possess it, is a publication of the Department of Commerce entitled "Circular of the Bureau of Standards No. 55, Measurements for the Household." This is an elaborate book of nearly one hundred and fifty pages on calendered paper, profusely illustrated and well indexed. It is concerned with the dissemination of information as to units, methods and instruments of measurements useful in household activities, with many associated facts of interest and value.

In this publication are described the use of scales, measures of volume, measures of length, instruments for measuring heat, light, electricity, gas, water, atmospheric humidity, atmospheric pressure, density of liquids and time.

Much scientific information of general value is interestingly given and this publication is worth many times the price of fifty cents, which is charged for it.

"Say it with flowers" has been paraphrased to "Say it with poison ivy" in case one wishes to put reverse English upon his compliments. How to recognize poison ivy and twenty-nine other poisonous plants of indigenous growth is made possible by the possession of *Farmers' Bulletin 86* of the United States Department of Agriculture, entitled "Thirty Poisonous Plants of the United States," by V. K. Chesnut. This bulletin contains an illustration of each of the plants, a description of it and the locality where it is likely to be found, together with a description of the symptoms of the poisonous effects produced.

If one is interested in being posted on house flies, and in learning how to get rid of them, if they neglect to wipe their feet before walking over the food, there are several government bulletins that will afford the opportunity. One of these is *Farmers Bulletin 459* on "House Flies," by L. O. Howard, which is an amplification of *Circular 71* of the Bureau of Entomology upon the same subject. It will surprise many readers of this bulletin to learn that the familiar house centipede or "thousand-legger," as it is usually called, is one of the natural enemies of the house fly and destroys large numbers of them.

The cockroach and the bedbug have their family history revealed and all of the intimate details of their lives exposed in *Circulars 51* and *47*, respectively, of the U. S. Department of Agriculture, Division of Entomology. Both of these pamphlets are by C. L. Marlatt, who seems to be better acquainted with these than most of us would care to be, judging from the thoroughness with which he discusses them. According to Mr. Marlatt, cockroaches are among the natural enemies of bedbugs and rapidly exterminate them when given an opportunity, but as the means of bringing them together is not suggested the statement loses some of its value. Perhaps the remedy would be to sleep in the kitchen and take one's meals in the bedroom in a house that happened to be doubly infested.

A very important publication dealing indirectly with the same subject is "*Circular 46* of the Bureau of Entomology, U. S. Department of Agriculture, on Hydrocyanic Acid Gas against Household Insects," by L. O. Howard.

This method of fumigation has upon numerous occasions been the cause of death of those who attempted to carry out the operation without realizing its dangers. Inasmuch as the pharmacist is the one who is usually called upon to supply the materials to be used for this method of fumigation, it is reasonable to expect of him that he should have authoritative knowledge upon the subject and be prepared to give advice as to the details of carrying out the process with a minimum of danger.

*Farmers' Bulletin 127* deals with "Important Insecticides" in general and is by C. L. Marlatt. In it are discussed at length the methods of preparing and using all of the commonly used insecticide sprays, washes, vapors, soaps and oils. The usefulness of this bulletin will be more apparent to the country pharmacist than to his city brother, for it is in the country that Bordeaux mixture, lime-sulphur spray and kerosene emulsion are more frequently called for.

The foregoing are just a few scattered examples taken from the writer's collection of similar publications which has been accumulating for years and which has been found to be of great and continual value. To those who contemplate starting a collection of this kind it may be suggested that upon application to the Superintendent of Documents, there will be sent free of charge a complete index of government publications with prices thereof. To those who, having established such a collection, wish to keep it up to date, a monthly index will be sent containing lists of new bulletins, circulars, etc., as issued.

This is one of the neglected or unrecognized opportunities which, when properly taken advantage of, will yield returns both in money and in prestige to the pharmacist who takes the time and trouble to make such a collection and use it.

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## NOTES ON HENNA.

BY BENJAMIN H. HOFFSTEIN, Ph.C.

Despite the fact that Henna has been in use for some thousand years, the literature dealing with its various compounds and uses is scattered and fragmentary. The various compounds of Henna have

indeed been neglected, this prompted the research in literature, analysis and experimentation contained in this paper.

The word "Henna," which means "to become queen" is indicative of something highly elegant.

The drug known as "Henna" is derived from the plant *Lawsonia inermis*, Fam. *Lythraceae*. Some botanists recognize but one species, the *L. alba* with two varieties, *L. inermis* and *L. spinosa*; others indicate the fact that the young Henna plants are devoid of spines while the older plants have branchlets which have hardened into spines and so belong to the same variety of *Lawsonia*. *Ligusturum Egypticum* is a latinized English synonym for Henna, arising from the common name for the same in England, that of Egyptian Privet. This synonym is quite erroneous since it places the *L. inermis* in the group of Privets to which it does not belong.

Henna assumes quite a variety of names according to the country in which this plant grows. In Persia, it is known as "Henna," in Egypt the plant is called "Khenna," in Arabia it is known as "Alkhenna," in India it is called "Mendeed" and in the West Indies where the plant has been naturalized, it is known as "Jamaica Mignonette."

*L. inermis* is of a slender shrubby nature, from about eight to eleven feet in height, bearing smooth, opposite, lance-shaped leaves, with entire margins. The flowers are small and white, with four petals and are devoid of panicles. They possess a very pleasing odor. The drug on the market consists of the leaves and twigs of *L. inermis* and is of ancient repute as a cosmetic and active medicinal agent in the countries to which it is indigenous.

The primordial use of Henna appears to have been more a matter of hygiene than that of augmenting beauty. The aqueous infusion of the leaves applied to the external surfaces of the body was used as a prophylactic against certain skin diseases which are quite prevalent in the eastern tropical and semi-tropical countries. Another property of this infusion was said to be that of producing a cooling sensation to the part applied, acting gently on the sweat-glands, reducing their activity, benefiting both health and comfort. The root of the henna plant was upheld as a specific in leprosy and also in drying up certain ulcers of the mouth and gums. The flowers of the plant are still used in preparing a delicate highly esteemed perfume of the East said to be equal in aroma to our lilac. The fruit is claimed to be an emmenagogue.

The most common use of Henna among the ancients was that of a dye. Among the Mohammedans, both men and women used it and those that did not employ it were considered indecent. In China the infusion is used to paint an orange red line underneath the eyebrows, and so considered as an aid to beauty. In most of the Mohammedan countries, the hair, soles of the feet, palms of the hands and finger-nails were stained an orange red color by an aqueous infusion of this drug. That this practice had been carried on in the remote ages is shown by the color of the various parts of the bodies of the old Egyptian mummies. Henna was also used to color the manes and tails of horses.

The Ancients made an aqueous infusion of the powdered leaves and twigs of henna and dyed the hair a light auburn color. The darker gradations of this color were brought about by the use of infusions of catechu or lucerne (Alfalfa) leaves. Vinegar and alum water were used in combination to produce darker auburn shades, at the same time acting as mordants. However, the color of Henna without the use of mordants lasted three or four weeks despite the frequent use of baths.

The coloring value was taken advantage of in staining various skins and soft leathers an orange red color as well as in staining certain woods of light shades a mahogany color. The use of Henna in dyeing wool and silk has also been reported favorable and staple shades have been produced with various mordants.

For the dyeing of hair the market at present offers two varieties of powdered Henna, namely, an Egyptian and Arabian variety. The Arabian is more esteemed but before it comes into the market it is adulterated with sand to make it of equal coloring virtue to the Egyptian. In Turkey the powdered leaves of *Anchusa tinctoria* are said to be substituted for Henna.

Returning to our present day we find that the use of Henna as a recoloring for hair is still being used by a number of people, producing the Titian and Henna shades, by the following procedure:

About 200 Gms. of drug is used for one application. This is divided into two portions. With portion No. 1 an aqueous infusion is made, using one pint of boiling water. This infusion must be used while still hot and applied with a brush. With portion No. 2 make a moderate thick paste using water. Apply to the hair and hold in place with a towel wrapped around the head. Allow to remain for thirty minutes. Then rinse the hair in tepid water, a recoloring being necessary within about thirty days.

There are, however, on the market at the present time a large number of so-called Henna Hair Dyes and Henna Hair Compounds producing as many as eleven different shades. Henna alone produces only a few shades in Auburn according to the concentration of the infusions. The many shades and colors produced by the numerous hair compounds mainly rely upon the leaves of *Indigofera tinctoria* known as "reng" for the production of dark colors, and the admixture of metallic salts with plant tannins to form inks. Among the common metallic salts used are  $\text{SnCl}_2$ ,  $\text{NiCl}_2$ ,  $\text{FeSO}_4$ ,  $\text{CuSO}_4$ .

In a recent analysis a guaranteed Henna hair compound, considered to be one of the best on the market disclosed the following combination: Powdered Sumach, Henna,  $\text{FeSO}_4$ ,  $\text{CuSO}_4$ . These ingredients were placed in the container in layers. The Sumach admixed with small quantity of Henna made up the lower layer. The metallic salts in a powdered form were admixed with 50 per cent. of Powdered Henna making up the second layer and the top layer consisted of Powdered Henna leaves. The directions indicated the use of the entire contents of the container at one application. These ingredients made up ten shades of dye being admixed in different proportions. The blond color of this dye was suspected to contain a mixture of Henna and Picric Acid, the latter being present to the extent of one-half per cent. The coloring in this set of hair dye was dependent upon the tannin found in Sumach and Henna which produced inks with the metallic salts of copper and iron; at the same time these metallic salts acted as mordants to the dye principle present in Henna.

Another analysis of a different set of dye contained a mixture of Pyrogallol and Henna in one container and a mixture of Ammonium Chloride and Copper Sulphate in another. The Henna in this case made up about 2 per cent. of the mixture.

The Encyclopedia Britannica, 11 Edition, 1910-11 and Lindsley state that Henna contains no tannin and it appears that numerous other works have copied and recopied this statement which is erroneous.

According to the method of Herraony in the AMERICAN JOURNAL OF PHARMACY, Volume 35, page 177, a tannin can be extracted from Henna and this has been used to dye hair, being very efficient, acting in a shorter space of time than powdered Henna.

The method consists of extracting the chlorophyll of Henna with ether, then percolating the residue with 90 per cent. Alcohol, dis-



tilling off the Alcohol and again exhausting the syrupy residue with ether. The residue is dissolved in 95 per cent. alcohol which is again distilled off. This method yields a resinoid tannin soluble in hot water and capable of reacting with ferric salts and gelatin like other tannins. The originator of this method named the dye principle in Henna, Henna-tannic Acid.

BOTANICAL RESEARCH LABORATORY,  
PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE.

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SUGGESTIONS FOR UNITED STATES PHARMACOPOEIAL  
REVISION SUBMITTED BY THE COMMITTEE ON  
THE UNITED STATES PHARMACOPOEIA OF THE  
PHILADELPHIA COLLEGE OF PHARMACY.

MAY, 1920.

SCOPE AND GENERAL PRINCIPLES.

*Scope of the Pharmacopoeia.*—We recommend that the limitations applied against the admission of patented and proprietary preparations and medicinal substances in the U. S. P. IX, be continued in the next revision.

*The Diagnostical Reagents and Clinical Tests.*—We consider this as extra pharmacopoeial, not being within the scope of a book of standards for medicines, and the scope as defined in the U. S. P. IX, and therefore should be eliminated from the book.

*Posology.*—We recommend that there be established a special sub-committee on Posology of the Committee on Revision; further, that in place of the statement of average doses, as shown in the U. S. P. IX, there be given *a range of commonly prescribed doses for adults*, and that this be accompanied by a statement that the doses given are to be considered as advisory for the guidance of the physician, not as compulsory, or restricted doses.

In the interest of uniformity and accuracy, a standard dosage measure should be described by the U. S. P.

*Pharmacopoeia Titles for Synthetic Chemicals.*—We recommend that the Committee of Revision be given authority to coin short and euphonious names for synthetic chemicals, where the chemical name is too lengthy or unwieldy for a title, but that in all such cases the true chemical name be given as a synonym.

*Synonyms.*—Where several names are in extensive use in the drug trade, these should be given as official synonyms.

*Limitations of Purity.*—We recommend that the statement in the present revision, under the head "Purity and Strength of Pharmacopoeial Articles," be amended by eliminating the last clause relating to the standards of drugs in other countries.

*International Standards.*—While approving of the principle of International Standards for potent drugs and medicinal preparations, it is believed that the standards of the Brussels Conference of 1902 should receive careful revision, and that another International Conference should be convened for determining proper International Standards at this time.

*List of Official Preparations.*—We recommend that a statement of the preparations, in which the article is used, should be continued in the monographs, as in the last revision (U. S. P. IX).

*Alcoholic Percentages.*—We renew the recommendation that there should be added to each official liquid preparation containing alcohol a statement of the range of alcohol, by volume, contained in the product.

*Assay Processes.*—We urge the re-adoption, and putting into effect, of the recommendations that tests of identity and purity be given for determining the character of the products of Assays.

*Biologic Assays.*—These should be called Pharmacodynamic Tests, and should be admitted only where the standardizing of the drugs or preparations cannot be satisfactorily determined by chemical assays, and where the proposed methods for pharmacodynamic testing are sufficiently developed to yield concordant results.

*Serums and Bacterins.*—We recommend that the list of admissions of this class of Biologic Products be extended only where standards have been established by the proper governmental department.

*Weights and Measures.*—We recommend that the Metric System of Weights and Measures only should be used throughout the entire book.

*Supplements.*—The Executive Committee should again be empowered to issue supplements to the Pharmacopoeia, if, in their judgment, such be necessary.

*Publicity.*—We recommend that the Chairman of the Committee of Revision, with the approval of the Executive Committee, issue preliminary statements of the progress of the revision, and of the important changes contemplated.

*Atomic Weights.*—We recommend that the Atomic and Molecular Weights be based upon the latest available list of Atomic Weights, authorized by the International Committee on Atomic Weights.

*General Formulae.*—The introduction of General Formulae into the U. S. P. IX we believe has been entirely satisfactory, so far as applied. We recommend that the use of General Formulae be extended to every class of preparation where such a general treatment is possible.

*Physical Constants.*—We recommend that official methods for determining Physical Constants be given in the U. S. P. X, and the methods described in the U. S. P. IX should be extended and improved.

*Solubilities.*—It is recommended that the statements regarding Solubilities be extended to cover all of the more commonly used solvents.

*Standard Temperature.*—We recommend that the U. S. P. retain in the next revision 25° C. as the standard temperature, except in the case of alcohol.

*Compound Preparations.*—The introduction of formulas for new "Compound Preparations" should be discouraged.

*Pharmacognostical Descriptions.*—It is recommended by your Committee that the description of Crude Drugs, with brief pharmacognostical descriptions, both macroscopic and microscopic, as given in the many monographs of the U. S. P. IX, be extended to cover all drugs where the knowledge will permit of such pharmacognostical descriptions.

*Powdered and Ground Drugs.*—Wherever practicable, the ground or powdered drug should be required to represent the entire drug. Where the data available is sufficient to serve as a basis for a standard for allowable tailings, gruffs or residue, this should be determined and inserted in the text.

*Date When Official.*—It is recommended that the Committee of Revision continue the practice of printing upon the Title Page of the Pharmacopoeia a definite date when the revised Pharmacopoeia shall supersede the previous edition. Due consideration should be given to the time necessary to dispose of stocks on hand and to prepare new formulas for the trade. The period between the time when the book becomes available to the trade and when it becomes official shall be not less than six months.

## ADMISSIONS AND DELETIONS.

*Additions Recommended.*

Acetyl-Salicylic Acid  
 Arsphenamine  
 Barbital  
 Barbital Sodium  
 Barium Sulphate (Purified for X-Ray use)  
 Benzyl Alcohol  
 Benzyl Benzoate  
 Carrell-Dakin Solution  
 Chloramine-T  
 Chlorcosane  
 Chloretone  
 Di-Chloramine-T  
 Neoarsphenamine  
 Peanut Oil  
 PicROTOXIN  
 Physostigmine Sulphate  
 Procaine (Novocaine)  
 Scarlet Red  
 Silver Albuminate  
 Silver Nucleinate  
 Solution of Benzyl Benzoate (20 per cent.)  
 Tincture of Staphisagria

*Deletions Recommended.*

Aluminum Hydroxide  
 Ammoniated Glycyrrhizin  
 Bismuth and Ammonium Citrate  
 Ceylon Cinnamon  
 Chondrus  
 Cottonseed Oil  
 Effervescent Citrated Caffeine  
 Emulsion of Almond  
 Ethyl Carbamate  
 Fluidextract of Staphisagria  
 Glycerite of Hydrastis  
 Lithium Carbonate  
 Morphine (Alkaloid)  
 Saccharated Ferrous Carbonate  
 Serum Antidiphthericum  
 Serum Antitetanicum (The purified form has, in practice, entirely superseded the last two)  
 Sesame Oil  
 Solution of Sodium Glycerophosphate  
 Sweet Almond  
 Tincture of Lactucarium (If the Syrup is prepared from the drug)  
 Uranium Nitrate

## CHEMISTRY.

*Definitions and Derivations.*—It has been the custom of the U. S. P. to state the derivation of organic chemicals and to give some sort of a definition for this class of substances. Tartaric acid is described as "A dibasic organic acid, usually obtained from wine lees or argol." Quinine sulphate is defined as "The sulphate of the alkaloid quinine." Such statements and definitions might have been useful in the earlier revisions, but they are no longer needed. With the present official status of the U. S. P. statements of this kind, if strictly interpreted, may cause misunderstandings. Glycerin, for instance, is defined as "A liquid obtained by the hydrolysis of vegetable or animal fats, or fixed oils, purified by distillation." Would glycerin made by fermentation of sugar or from hydrocarbons (several patents claim the latter process) and purified by other means than distillation not be suitable for pharmaceutical use if it meets all purity requirements? The same applies to citric and tartaric acids, the latter of which may eventually be made from benzine, and to a number of other official organic chemicals.

It is quite safe to say that the average user of the Pharmacopoeia knows better what the sources of quinine or sugar are than those of acetic acid or ammonium chloride. The U. S. P. does not give the derivation of the latter two substances, yet apparently nobody missed it and it did not detract from the prestige and value of the book. For the purpose of the Pharmacopoeia, the derivation of a *definite* chemical substance, like the method of its manufacture, does not at all matter, provided, of course, it measures up to the U. S. P. specifications.

The definition of quinine sulphate as "The sulphate of the alkaloid quinine," and similar other definitions are tautologies. Sodium sulphate is not defined in the U. S. P. as the sulphate of the metal sodium. Why?

It is therefore recommended that in the next revision of the Pharmacopoeia derivations of *definite* chemical compounds and definitions of organic chemicals, of the character cited above, be omitted except when the definition is necessary for purposes of identification.

*Purity Rubrics.*—The object of purity rubrics and assays is to secure preparations and drugs of standard quality. If the same ends can be attained by the use of simpler tests, there is obviously no reason for employing difficult and laborious tests. This being granted, as a matter of course, several purity rubrics and assays could be advantageously omitted. No purity rubric of 99.5 per cent. or an assay is needed for mercury. If the mercury is of the proper appearance, it is necessarily more than 99.5 per cent. pure; in fact, it is nearly 100 per cent. pure. The assay of sulphur is a difficult one and not infrequently runs amuck. Is this assay really necessary to insure a product of the desired purity? The good appearance of the sulphur in connection with a limit for non-volatile matter, and a few more simple tests if needed, will insure as pure a product as is afforded by an assay. Why then burden the users of the Pharmacopoeia with unnecessary work? Most probably the assay of sulphur and a few other similar official assays are very little used and then only as a matter of formality.

*Tests for Impurities.*—In the Ninth Revision of the U. S. P. greater definiteness has been achieved in the description of chemical tests than in former revisions, but perfection has not been reached—if it ever will be. Because of the extensive and growing use of Pharmacopoeial standards and methods of testing, the tests for

impurities should be made of a more definite character wherever possible. Such expressions as "slightly acid," "slightly turbid," etc., have always been deprecated. They have been a source of uncertainty and worry to the conscientious, and, on the other hand, a good excuse for foisting on the public inferior products. With the number of persons engaged in testing U. S. P. preparations rapidly increasing, the possibilities of attaching different interpretations to these expressions is multiplied and it becomes very necessary to guard against it.

Quantitative or semi-quantitative tests should therefore be adopted for permissible impurities wherever such tests are available, when they are not difficult of execution, and can be made without the use of elaborate apparatus. For instance, instead of "slightly acid or slightly alkaline" a titrimetric limit for acidity or alkalinity should be given. Turbidimetric comparison tests can likewise be used for chlorides, sulphates, and similar impurities. These tests should preferably be described under a general heading in Part II, as the test for arsenic in the present edition. The advantage of this method is very obvious. The tests can be described with more detail and greater clearness, and thus promote greater accuracy and uniformity.

In describing tests for impurities, no detail should be omitted which is conducive to more harmonious results. As an example, the method of preparation of saturated solution of the substance to be tested may be cited. Not infrequently diametrically opposed reports have been made because of the different methods used in preparing the saturated solution.

In salts containing water of crystallization, the U. S. P. assays frequently fail in their object. A deficiency in purity may be concealed by a deficiency in water. For example, sodium phosphate or thiosulphate of sub-standard purity may still show the required purity of the assay and thus defeat the object of the U. S. P. To remedy this defect, it is suggested that suitable tests, limiting the proportion of such impurities as are likely to be present and are not taken care of by the assay, be introduced. In the instances cited above, a test for limit of sulphate will be appropriate. Another method to overcome this is to assay the dried (anhydrous) salt. The latter procedure, however, is not always practicable.

*Assays.*—The introduction in the Ninth Revision of the U. S. P. of general assays for alkali salts of organic acids and for halogen

salts has proved very satisfactory. It is recommended that this be extended to other assays which are frequently used in the U. S. P., such as tests for acids, ferric salts, zinc salts, benzoates, and salicylates.

It is further suggested that wherever such assays are available and are not unduly laborious, the active principle of the substances be determined. In calcium chloride the calcium should be estimated and in sodium benzoate and salicylate the respective acid determined. The correctness of this recommendation is self-evident.

*Test for Zinc.*—The U. S. P. test for heavy metals takes no cognizance of zinc. Although contamination of U. S. P. products with this metal is not of frequent occurrence, it is desirable to make provision against its presence in undue proportions. It is therefore recommended that a test for zinc be included in the heavy metals test.

*Drying to Constant Weight.*—It is highly desirable that this expression, so frequently used in the Pharmacopoeia, be defined. A definition of this term will be of particular value in the determination of water in soaps and other products of similar character. It is impossible to *strictly* dry soap to constant weight. After the water has been presumably expelled, soap will keep on losing in weight to a small extent on further drying, and occasionally a gain in weight has also been noted. A definition along the following lines might answer. The expression "*dried to constant weight*" is intended to mean that two consecutive weighings, after drying for an additional hour, do not differ by more than 0.1 per cent.

*Unweighable.*—It is recommended that the term "negligible" be used instead of "unweighable," retaining for it the same definition as is now used for unweighable.

*Test Solutions.*—The majority of U. S. P. test solutions are made up to 10 per cent. regardless of whether the substance is anhydrous or contains 60 per cent. of water. The solutions bear no relation to each other. This is not in keeping with good scientific practice. It will suffice to note that whereas diluted hydrochloric acid is nearly triple normal, diluted nitric acid is  $1\frac{1}{2}$  normal and diluted sulphuric acid is double normal. It is recommended that in the next revision test solutions be prepared on the normality basis. The advantages of this system are very obvious. As a matter of fact, this is not an innovation. Several of the test solutions now official—silver nitrate T. S., potassium permanganate T. S., sulphocyanate, and sodium thiosulphate, are made up on normality basis.

*Volumetric Solutions.*—It is further suggested that the "V. S." following the designation of the normality, e.g., "tenth-normal sulphuric acid V. S.," be omitted. It is practically tautology.

*Thermometers.*—The thermometers official in the present U. S. P. are almost unobtainable and furthermore there seems to be no need for several of the thermometers specified. It is suggested that in the next revision a more readily obtainable type of thermometer be adopted and their number reduced to a more practical basis.

#### BOTANY AND PHARMACOGNOSY.

The following recommendations are respectfully submitted to the General Committee:

1. That the Sub-Committee on Botany and Pharmacognosy be given authority to investigate the source of certain official substances like Saigon Cinnamon, Asafoetida, etc., which are at present of either indefinite or partly indefinite origins.

2. That this Sub-committee make a searching inquiry into plant names that are adopted to represent the botanical origins of vegetable drugs, to determine priority in accordance with the Vienna Code.

3. That histological descriptions be given in the text of the U. S. P. for all crude drugs considered therein, which possess cellular structure.

4. That the range in width of the medullary rays of various drugs be based on studies of longitudinal-tangential sections.

5. That the limit of ash for all drugs be revised in accordance with the latest data.

6. That the family name be the sole group name to follow natural origins in the drafting of official definitions for drugs of vegetable or animal source.

7. That the list of plant synonyms be carefully revised.

8. That a limit of impurities be stated in the definition for *Prunus Virginiana* and that this be fixed tentatively as "not more than 3 per cent. of wood or other foreign matter."

9. That a determination of the crude fiber allowable in powdered wild cherry bark be made, to the end that a limit of impurities be placed on the powdered or ground drug.

10. That the term "micron" be employed in the next revision of the U. S. P. in place of "millimeter (mm.);" for designating the size of microscopic objects and that a statement be placed in the



Preface as to the reason for this change, which is that the micron is the standard unit of microscopic measurement.

11. That a limit for extraneous matter be fixed by the U. S. P. in each definition of a vegetable drug where such contamination is unavoidable.

#### NOMENCLATURE.

The following suggestions are respectfully submitted for consideration:

1. That the general style of the present Pharmacopoeia in the arrangement of Latin and English titles and of synonyms and abbreviations be continued.

2. That changes in official titles, Latin or English, be made only for very important reasons and that conservatism be the basic policy in dealing with all propositions which involve changes in titles which have already become more or less fixed by custom.

3. That in the adoption of new official titles, practical consideration, especially with reference to their use in prescriptions, be deemed of greater importance than matters of etymology, or of classical analogy.

4. That with the introduction of new drugs, which have entered commerce under a vernacular title, the names be in every instance Latinized by the appending of a Latin ending, and not introduced unchanged as Latin titles in the Pharmacopoeia, to be classified as indeclinable nouns. In other words, that the list of indeclinable nouns like Buchu, Gambir, Sumbul, etc., be not extended. This recommendation does not, however, imply the suggestion that indeclinable nouns already in the Pharmacopoeia be changed.

5. That when a new chemical is made official, the name be Latinized by adding the termination, either "a" or "um," according to analogy or according to the nature of the chemical in question.

That means that third declension endings be avoided and that the names of newly added chemicals be given terminations which will relegate them either to the first or to the second declension. This practice will greatly facilitate correct usage in prescription writing.

6. That cumbersome chemical names, such as Sulphonethylmethanum, which cannot be expected to become an integral part of prescription nomenclature, be avoided, and that short coined names be used instead.

7. That the spelling of "gramme" be retained for the unit of metric weight, to avoid confusion with "grain" in handwritten formulas and prescriptions.

8. That the term "Mil" as the unit of liquid measure be continued.

9. That in the constructing of new titles, either for chemicals or preparations, the use of names which are therapeutically suggestive, be avoided; but this suggestion does not imply that we favor the replacing of such well-fixed titles as compound cathartic pills.

10. That the abbreviations given under the official title in each monograph in the U. S. P. be carefully revised. It would seem to us that abbreviations which go no further than the dropping of a final "a" or any other declension ending, should be avoided.

11. That Latin titles in the index be accented, or that a complete list be printed of all official Latin titles with the accent indicated, or better, with accent and diacritical marks in conformity with the English pronunciation of Latin words.

A list of the Latin titles of the U. S. P. IX, with accents indicated, as suggested by Wallace S. Truesdell, A.M., Instructor in Latin at the Philadelphia College of Pharmacy, is herewith appended with the hope that it may be of assistance in the next revision.

12. We recommend that the title "Virus Vaccinicum" be replaced by the title "Virus Vaccinum." That the title "Serum Antidiphthericum" be replaced by "Antitoxinum Diphthericum." That the title "Serum Antitetanicum" be replaced by "Antitoxinum Tetanicum." That the adjective "purificatum" be avoided in the titles of sera and antitoxins.

#### GALENICALS.

*Acidum Hydriodicum Dilutum.*—The heating of the solution of potassium salts seems to be unnecessary. The directions to heat should be omitted.

*Aquae Aromaticae.*—The use of insoluble distributing substances of all kinds (purified talc, purified siliceous earth, and filter paper), should be omitted from the general process, and the direct addition of the medication to the distilled water, and the distillation method only be retained. By the direct addition of volatile oils, creosote, powdered camphor, etc., satisfactory waters may be prepared and the contamination which so often results from the use of these foreign

agents be avoided. Waters made in this way may be truly sterile and will keep much better than when made by the present general formula.

*Ceratum Cantharidis*.—If practicable a physiological test for the activity of cantharides cerate should be introduced.

*Ceratum Resinae*.—There should be a slight change in the directions so that the rosin will not separate during cooling. It would be better to direct that when the melted mixture is strained, it be stirred continuously until it starts to congeal.

*Elixir Aromaticum*.—The use of purified siliceous earth is preferable to purified talc, as it filters more rapidly and produces a brilliantly clear elixir.

*Extractum Cannabis*.—Glucose is not a satisfactory diluent because of the resinous character of this extract. It is suggested that rosin or some other more suitable substance be experimented with as a diluent.

*Glyceritum Acidi Tannici*.—The direction to strain the solution through cotton, while warm, is impracticable. The agitation of the mixture in a wide-mouthed bottle, is also difficult. It would be better to stir it with a heavy glass rod or wooden paddle.

*Infusum Digitalis*.—Reintroduce the 10 per cent. of alcohol, heretofore directed for infusion of digitalis. The infusion as now prepared often ferments before the patient can use all of it, and the small percentage of alcohol is not objectionable.

*Linimentum Ammoniae*.—Peanut oil can very satisfactorily replace oil of sesame. The latter oil is difficult to obtain and expensive, as it is imported, and peanut oil produces a superior emulsion and is an American product.

*Linimentum Camphorae*.—Peanut oil can also be used in this liniment to advantage, replacing the cottonseed oil which is a semi-drying oil and unsatisfactory for external application. It would be desirable to introduce here a more practicable assay. The evaporation method is sufficiently accurate and may be easily applied without special apparatus.

*Liquor Cresolis Compositus*.—The formula submitted by Mr. Samuel L. Hilton (*J. A. Ph. A.*, p. 759, 1919), directing the use of sodium hydroxide and oleic acid for the extemporaneous preparation of soap in this solution, is approved. The formula is as follows:

Cresol.....	500 Gms.
Oleic Acid.....	226 Gms.
Sodium Hydroxide.....	35 Gms.
Water, sufficient to make.....	1000 Gms.

Dissolve the sodium hydroxide in 100 Mils of water and filter the solution through asbestos. Weigh the oleic acid in a tared vessel, add the cresol, and stir thoroughly. Now add the solution of sodium hydroxide, stir vigorously until saponification occurs, and finally add sufficient water to make the solution weigh 1000 Gms.

*Liquor Ferri Chloridi.*—This solution is described as “reddish brown” in color. It is more nearly “yellowish brown.”

*Liquor Ferri Tersulphatis.*—The description here is “yellowish brown.” It should be “reddish brown.” The color descriptions of these two solutions were evidently confused.

*Liquor Formaldehydi.*—Methyl alcohol is specified in this solution, to prevent polymerization. It would be desirable to permit the use of either methyl or ethyl alcohol.

*Liquor Magnesii Citratis.*—The use of talc in this solution is unnecessary and undesirable. Partial sterilization of the product, as directed in the present Pharmacopoeia, is unnecessary when the solution is sold within a few days, and only adds to the time necessary for its preparation. If the solution is to be kept for any length of time, it should then be properly sterilized. This can best be accomplished by heating the completed solution in stoppered bottles in an Arnold sterilizer, or steam boiler.

*Liquor Plumbi Subacetatis.*—This preparation may be made equally satisfactory by mixing the lead oxide with the solution of lead acetate, agitating occasionally during seven days and filtering. Heating for one hour evaporates the solution continuously, necessitating the addition of more water and usually causing considerable precipitation of lead as carbonate. The cold maceration method has been used for a number of years in large laboratories and also on a small scale and the resulting product frequently tested and found to be identical with that prepared by the hot process.

*Magma Magnesiae.*—The suggestion of Sister Bertha Mueller (THIS JOURNAL, p. 162, 1920), that this magma be made by triturating commercial light magnesium oxide with lime water, has been found an improvement over the present official method and should be carefully tested for possible U. S. P. use. The minute quantity of calcium present is not objectionable and all washing of the magma is avoided. The formula is as follows:

Light Magnesium Oxide, U. S. P.....	60 Gms.
Solution of Calcium Hydroxide, U. S. P., sufficient to make.....	1000 Mils

Add the light magnesium oxide gradually and with constant stirring to 800 Mils of the solution of calcium hydroxide, contained in a graduated jar of at least double the capacity required for the mixture. Then add enough of the solution of calcium hydroxide to make the product measure 1000 Mils and shake or stir the mixture vigorously at frequent intervals until it has thickened properly.

*Mistura Cretae*.—This mixture can be prepared so that it is permanent and ready for instant dispensing, as follows:

Add 1 Mil of oil of cinnamon to 200 Gms. of compound chalk powder. Gradually and thoroughly triturate this powder with 400 Mils of cinnamon water. Transfer the mixture to a graduated bottle and add sufficient cinnamon water to make the product measure 1000 Mils. The preparation of this mixture before actually needed usually assures a more perfect suspension of the chalk, due to more careful trituration. The added oil preserves the mixture indefinitely and increases its palatability. The mixture is ready for instant dispensing and will not ferment within a few hours when kept by the patient, as frequently occurs when the official mixture is dispensed. This new formula has been tried under all manner of store conditions and temperatures, and has been found to keep indefinitely.

*Mucilago Acaciae*.—It is suggested that the official mucilage be made extemporaneously from granulated acacia. This is the almost universal custom and if a granulated acacia is selected, of official quality, the product is entirely satisfactory.

*Oleoresins*.—The Pharmacopoeia has alternated on the solvent used for oleoresins in each of the recent revisions. In one decade it was acetone, in the next, ether, for all of the oleoresins except cubeb. It is suggested that either solvent be directed, except in oleoresin of cubeb, as they seem to be identical in action. This will permit the use of the one which is readily obtainable or the one which is most economical.

*Oleum Aurantii and Oleum Limonis*.—The addition of 5 per cent. of a fixed oil, preferably olive oil, to these citrus oils, has been found to preserve them indefinitely from the development of turpentine-odor. There would be no serious objection to the Pharmacopoeia recognizing this method of preservation, as it would mean the use of oils of satisfactory quality in elixirs and elsewhere, instead of the frequent employment of oils having a turpentine-like odor. The added olive oil would separate from most of the mixtures and could

be filtered out. The percentage which is used could easily be checked by an evaporation test. Samples preserved in this way under the most trying conditions have kept for more than ten years. The same oil unpreserved became turpentine-like in a short time.

*Phenol Liquefactum*.—Add the following note to the official text:

When phenol is to be mixed with collodium, fixed oils, or petrolatum, use melted crystalline phenol instead of liquefied phenol.

*Spiritus Aetheris Nitrosi*.—The manufacturing process of the U. S. P. for spirit of nitrous ether should be omitted. There should be included in the U. S. P. a standard for ethyl nitrite as now sold. The spirit of nitrous ether of the U. S. P. should then be directed to be made from definite weights of this standard ethyl nitrite and of alcohol.

*Syrupus Aurautic*.—It is recommended that the talc be omitted and the following formula used:

Tincture of Sweet Orange Peel.....	50 Mils
Citric Acid.....	5 Gms.
Glycerin.....	100 Mils
Syrup, sufficient to make.....	1000 Mils

Mix the tincture with the glycerin and then add the syrup in which the acid has been dissolved. The syrup is not entirely clear but its flavor is superior to that prepared by the U. S. P. IX method.

*Syrupus Hypophosphitum*.—Direct the calcium hypophosphite to be dissolved in the water with the aid of the hypophosphorous acid as the first step in the making of the syrup; otherwise there is often difficulty experienced in obtaining its solution.

*Syrupus Ipecacuanhae*.—Acetic acid should be omitted from the formula, as hydrochloric acid is used in the fluidextract when made according to the Pharmacopoeia formula.

*Syrupus Lactucarii*.—We recommend the process for this syrup suggested by Beringer (THIS JOURNAL, p. 315, 1909), as follows:

Las ucarium.....	50 Gms.
Glycerin.....	250 Mils
Sugar.....	600 Gms.
Stronger Orange Flower Water.....	100 Mils
Distilled Water, sufficient to make.....	1000 Mils

Mix the lactucarium with 400 Gms. of clean sand by thorough trituration. Place the mixture in a percolator, and without packing, pour on sufficient of a mixture of the glycerin, orange flower water,

and 300 Mils of distilled water to saturate the powder had leave a stratum above. Close the percolator and macerate the drug for two days. Then percolate slowly, using the remainder of the mixture and afterward sufficient distilled water to yield 700 Mils of percolate. Dissolve the sugar in this percolate with the aid of the heat of a water bath, strain if necessary, and finally add sufficient distilled water to make 1000 mils.

*Syrupus Senegae*.—The present U. S. P. product is unsatisfactory because it frequently precipitates. The direct addition of the fluid-extract to syrup naturally causes this difficulty. A far superior syrup, pharmaceutically, can be produced by the process suggested by Beringer (THIS JOURNAL, p. 320, 1909), as follows:

Senega, No. 20 powder.....	200 Gms.
Ammonia Water.....	20 Mils
Glycerin.....	100 Mils
Sugar .....	750 Gms.
Water, a sufficient quantity to make.....	1000 Mils

Mix the ammonia water and glycerin with 200 Mils of distilled water, moisten the drug with sufficient of this menstrum, and pack it lightly in a percolator. Allow the moist drug to macerate for twenty-four hours, and then percolate into a receiving vessel, graduated to 800 Mils, and containing the sugar; use first the remainder of the menstrum and then sufficient water to make the sugar and percolate measure 800 Mils. Reserve this portion and continue the percolation with chloroform water until the drug is exhausted. Evaporate this second percolate to 200 Mils, add it to the reserved portion, agitate until the sugar is dissolved, strain the syrup, and add sufficient water to make the product measure 1000 Mils.

*Tinctura Zingiberis*.—It has been shown that 75 per cent. alcohol extracts all of the active constituents of tincture of ginger. The resulting product will have to be restandardized from the standpoint of maximum and minimum extraction.

*Troches*.—Troches should be either omitted from the Pharmacopoeia or modernized as to flavor and size. The principle of making all troches 1 Gm. in weight has proven very satisfactory in the N. F. The cubeb troche is probably the only one of the official troches which is needed.

*Unguentum*.—Yellow wax produces a better product than white wax, and the color is not objectionable. The ointment is smoother and seems to be preserved more satisfactorily.

*Unguentum Acidi Borici*.—Paraffin is not a satisfactory hardening agent in this ointment. White wax or spermaceti would be better. Paraffin always causes the ointment to become granular.

*Unguentum Aquae Rosae*.—The expressed oil of apricot kernels should be recognized by the Pharmacopoeia and used in this ointment. This expressed oil is an American product, seems to be as satisfactory as expressed oil of almond, and is much less costly. As a matter of fact, it is probably used in the preparation of this ointment in most instances at the present time, and its use should be acknowledged.

*Unguentum Belladonnae*.—The addition of 5 per cent. of yellow wax to this ointment, replacing an equivalent amount of benzoinated lard, greatly improves the product, which is usually too soft.

*Unguentum Chrysarobini*.—Omit the directions to strain the product, as this seems to be unnecessary and an undesirable manipulation.

*Unguentum Diachylon*.—It ought not to be necessary to strain the lead plaster and petrolatum in this ointment.

*Unguentum Hydrargyri Dilutum*.—This ointment has been found to be too soft in consistence for normal conditions. By replacing 40 Gms. of the petrolatum with yellow wax, a more satisfactory product is obtained.

*Unguentum Hydrargyri Nitratis*.—The formula given in the Pharmacopoeia is satisfactory for small lots of ointment. In the directions it should be made more clear that after the nitric acid is added to the melted lard, the heat should be very gradually increased until the characteristic reaction is complete. It is important also to state that the solution of mercuric nitrate should be incorporated with the nitric acid-treated lard before it has become cold.

*Unguentum Hydrargyri Oxidi Flavi*.—Ointment of yellow mercuric oxide is chiefly used for ophthalmic purposes and the strength is then about one per cent. An ointment of this strength should replace the official ointment or be introduced as a "diluted ointment of yellow mercuric oxide." This should be made with a petrolatum base.

*Unguentum Zinci Oxidi*.—Persistent efforts have been made to authorize the substitution of the benzoinated lard in this ointment with petrolatum. Doubtless superior keeping qualities are exhibited by the modification, but the therapeutic value of the ointment is changed. It has been repeatedly observed by physicians



that this ointment owes its value as a healing ointment to the fact that the lard vehicle is quickly absorbed, leaving the coating of zinc oxide which exerts astringent and healing effects. On the other hand, when petrolatum is used, the surface remains moist, and the chafing on a skin surface is not relieved. The present official ointment should be made from a benzoinated lard of high quality, practically anhydrous, and if so prepared, and especially if preserved in tubes, it will keep for a long time without becoming granular.

*(To be continued.)*

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## WHAT OF THE DAY? AND WHAT OF THE FUTURE IN PHARMACY?\*

BY HENRY M. WHELPLEY, M.D., PH.M.

ST. LOUIS, MO.

We are living in a day of industrial, economic and social relations, new to even the older ones in the present generation. The World War set in motion waves of human thought which are difficult to measure and impossible to escape. The wage earners have raced with the profiteers in an effort to outdo each other in extravagance. The demand for non-essentials has taxed the capacity of production. This has reduced the facilities and available labor for the production of essentials until prices have reached fabulous figures. The man of salary has been caught between two millstones and is now a pitiable looking individual of tattered and torn clothing and body.

The mind of man has a black reversion to selfishness in great contrast with the humanitarian spirit of pre-war days.

We fought for a larger cycle of liberty of human thought and action. We are now fettered and burdened in a way and to an extent that is difficult to comprehend. We are ready to admit the possibility of the incredible.

Such is the day during which we live and move and have our being at the time of the forty-second annual meeting of the Missouri Pharmaceutical Association.

Will our successors of the next generation look back on us with pity or with an expression of envy of "the good times they had but knew not?"

\* Read at the 1920 meeting of the Missouri Pharmaceutical Association.

I dare not hazard a guess in answer. I will say that we can make no calculation for the effective operation of the human mind nor set bounds to its operation. It is difficult to separate the psychological from the material features of the situation. But we feel safer in analyzing the economic condition.

A lull in the retail demand is sufficiently general to attract our attention. The highest priced goods are not bought with the recklessness that they were a month ago.

A credit strain, first acute in the East, has spread far westward. A reaction is at hand. But neither the true nature nor the full extent can be stated with certainty. Please do not say nor even think "calamity howler." That is just what I am anxious to counteract. This is no time to rock the boat.

Cool, deliberate judgment is now at a premium. The situation is aggravated by magnification and made more dangerous if belittled. The real truth of the situation may not be apparent any more than was the outcome of a great battle on the eve of a conflict. But what goes up must come down, and prices must, somehow, recede. Now, what of the future in pharmacy? That depends on the good judgment and wise action of those who are in business to-day.

Druggists are by education and training taught to be cool, but alert in time of accident and emergency. Their daily work has to do with human lives which are in the balance.

Of all in the commercial world, none is so well fitted as the druggist to help the pendulum swing back, slowly and safely, until deflation reaches a point where normal conditions staple equilibrium.

This is a time for action rather than high-sounding statements.

Never be out of staple goods if you can obtain them. Buy less luxuries and discourage their sale.

Collect with vigor all accounts.

Refuse long credits and avoid even short ones, in so far as you can.

Discount all of your bills. Do this even though you must burn less gasoline in order to find the money to meet business obligations.

The realm of human activities to-day does not present more worthy opportunities than those now before you for superior and laudable achievement in guiding along safe and sane lines the process of retrenchment not yet everywhere apparent. Help hold down

speculation, but believe that legitimate business must and will go on. Use your efforts to bring about recessions in an orderly manner. Carry the message of thrift and reduction into every drug store, not only of Missouri, but of this great country where resources and markets are enormous when compared with any other country of the world.

Do this, and when we hear the cry, "Watchman, what of the night?" the answer will be, "All is well in drugdom."

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## PHARMACEUTICAL EVENTS IN 1870.\*

BY OTTO RAUBENHEIMER, PH.M.

BROOKLYN, N. Y.

In connection with the Golden Jubilee of the New Jersey Pharmaceutical Association it might be of interest to learn what other important events in the field of pharmacy and allied sciences have taken place in 1870, the year of the birth of the Association. The arrangement of the paper, in conformity with a number of others presented at the Historical Section of the A. Ph. A. on the subject "Pharmaceutical Events a Century Ago," is as follows:

1. Of General Interest.
2. Events, Pharmaceutical, Chemical, etc.
3. Inventions and discoveries.
4. Bibliography.
5. Pharmacists and others born in 1870.
6. Pharmacists and others who died in 1870.

### OF GENERAL INTEREST.

March 30, 1870—the 15th Amendment of the Constitution of the United States was ratified, *viz.*:

"The right of citizens of the United States to vote shall not be denied or abridged by the United States or by any State, on account of race, color, or previous conditions of servitude."

May 25—Organization of English Committee to revise an authorized version of the Bible.

\* Read at the meeting of the New Jersey Pharmaceutical Association, Newark, June, 1920.

July 19.—France declares war on Prussia and the Franco-German war began.

Dec. 25.—Mount Cenis tunnel completed and becomes the principal route of transportation, also of drugs between Italy and Western Europe.

#### EVENTS PHARMACEUTICAL, ETC.

Above all the New Jersey Pharmacuetical Association was founded in 1870 and has been in existence uninterruptedly ever since. This event is undoubtedly presented in another paper at the Golden Jubilee.

In the same year the West Virginia and also the Vermont State Pharmaceutical Associations were formed. As a matter of record I might mention that the California Pharmaceutical Association was established in 1869 and the one of Maine in 1867.

Allgemeiner Deutscher Pharmazeuten Verein, the association of German drug clerks, was constituted on January 4, 1870. In 1900 its name was changed to Pharmazeutische Vereinigung.

The U. S. P. Convention, or as it was then called, National Convention of 1870 for Revising the Pharmacopoeia, was held in Washington on May 4. In the committee of 15 only 4 pharmacists were represented, namely, John M. Maisch, of Philadelphia, Albert E. Ebert, of Chicago, J. R. Moore, of Baltimore, and G. F. H. Markoe, of Boston.

Anton Schürer von Waldheim acts as representative and later as director of the Allgemeiner Oesterreichischer Apotheker Verein, the Austrian Pharmaceutical Society. He gained international fame by his project of an International Pharmacopoeia, for which he submitted a draft at the International Congress of Pharmacy at Brussels in 1885.

Rhode Island Pharmacy Law was enacted.

Dr. William Simon (1844–1916) professor of chemistry in Baltimore and well known to the pharmaceutical and medical and dental professions, came to the United States from Germany.

Frederick August Flueckiger, pharmacist, chemist, and above all pharmacognosist, was appointed extraordinary professor at the University of Bern, Switzerland.

Daniel Hanbury, the English pharmacognosist, retires from retail pharmacy in London. The Hanbury medal and Flückiger-Hanbury's Pharmacographia are living testimonials.

Still another pharmacognosist, Prof. August Wiggers, of Göttingen was honored by the so-called Wiggers Stiftung, an endowment for pharmacy students.

Ferdinand Tiemann, discoverer of synthetic Vanillin from Coniferin, became assistant to August Wilhelm Hofmann, professor of chemistry, University of Berlin, the discoverer of fuchsin (1858), which laid the foundation for the aniline industry in Germany.

George M. Ebers was appointed professor at the University of Leipzig. This egyptologist became famous through finding and acquiring the Papyrus Ebers in 1872 in Thebes, which formulary was written about 1600 B.C. and serves as an excellent illustration of the old Egyptian materia medica.

Oswald Schmiedeberg, the celebrated pharmacologist of digitalis fame, was called to a professorship at the University Dorpat.

#### INVENTIONS AND DISCOVERIES.

Condurango, long a household remedy in the northern part of South America, against snake bites, cancerous and syphilitic diseases, was introduced into the materia medica of the United States by Drs. Caesares and Equigureu, of Loja, and Dr. Thomas Antisel, of Washington, D. C.

In March, 1870, Cloëz reports in *Journal de Pharmacie et de Chimie*, 4 series XII, 291, an elaborate study of Eucalyptus leaves. The drug was then introduced into medicine and the tree was planted in malarial districts.

The manufacture of Sulphuric Acid Anhydride,  $\text{SO}_3$ , began by Cl. Winter, in Freiburg, Saxony, and by Messel & Squire, near London.

Marcellin Berthelot, pharmacien, professor, senator and member of cabinet, synthesized Benzene or Benzol,  $\text{C}_6\text{H}_6$ .

Friedel and Craft synthesized aromatic hydrocarbons.

C. Gräbe, of Geneva, determined the constitution of Anthracene and Phenanthrene.

Oswald Hesse discovers four more alkaloids in opium, namely, codamine, Laudamine, Lanthopine and Meconidine.

Hesse determines the molecular formula of the opium alkaloid Thebaine, isolated by Thibourney in 1835, as  $\text{C}_{19}\text{H}_{23}\text{O}_3\text{N}$ .

Hesse also determines the constitution of Narcotine.

C. R. A. Wright completes his researches on the chemical structure of Morphine, began in 1860.

S. M. Jorgensen, of Copenhagen, introduces the polyiodide test for the detection of alkaloids.

Dr. Wilhlem von Brugge (1819-92), professor of physiology at Vienna, introduces emulsion test for fatty acids.

Prof. Adolf von Baeyer, of Munich, of synthetic indigo fame, works on Mellitic Acid, on Purine derivatives and Uric Acid. He determines the constitution of Furfural and Pyrrol and invents the process of the formation of Hydrocarbons by reduction with Hydriodic Acid and Phosphorus.

Justus von Liebig, the father of agricultural chemistry, discovers Invertase. He also publishes his last book of importance "Über Lösung und Quelle der Muskelkraft."

J. Lothar Meyer (1830-95), professor at Karlsruhe and later at Tübingen, works on molecular volume and completes his researches on the periodic system, began in 1861.

Oskar Liebreich, dozent and later professor of pharmacology, Univ. Berlin, determines the structure of Betaine, the alkaloid in beet-juice, discovered by Scheibler in 1866.

Prof. L. I. Mendeleeff, of St. Petersburg, begins his work on critical data of gases, 1870-85.

Prof. Robert Wilhelm Bunsen, at Heidelberg, of "Bunsen-burner fame," invents Ice Calorimeter, an apparatus for determining specific and latent heat of bodies.

Ethylidine Chloride or Ethylene Chloride,  $\text{CH}_3\text{CHCl}_2$ , was introduced as an anesthetic by Prof. Bernhard von Langenbeck (1810-87), of Berlin, the greatest clinician, surgeon and teacher of his day in Germany.

Gelatin suppositories and Vaginal Globules introduced by Apotheker Grohs in Vienna, later Baron Grohs von Figely.

Petroleum burners replace the old Berzelius lamps.

Gruner recommends the steam turbine as a motor for the pharmaceutical laboratory.

Apotheker Reeb, of Strassburg, introduced oil and syrup shelf bottles with cup-shaped neck to collect the drippings.

Eugen Dieterich, of Helfenberg, manufactures paper bottle caps with a machine invented by Enzmann.

That even the Franco-German war acted as a stimulant to chemistry, pharmacy and medicine, can be seen from the following innovations.

Smokeless powder was invented.

Phosphorus Pills were issued against rats and mice.

Phenol, after being used as a disinfectant on the battlefield, came into general use.

Purified or Absorbent Cotton began to be used for dressing and Iron Chloride Cotton as a styptic.

Lana Pini, or Pine Needle Wool, was invented by Weiss, a paper manufacturer in Zuckmantel, Germany, and used as a substitute for the expensive cotton. Furthermore, two important industries were developed, the manufacture of pineneedle oil and pineneedle extract.

#### BIBLIOGRAPHY.

The publication of the Yearbook of Pharmacy of the Conference of the British Pharmaceutical Society was commenced.

British Homeopathic Pharmacopoeia published.

The 13th edition of the United States Dispensatory, containing 1800 pages, was published.

Franz L. Sonnenschein (1817-79), apotheker and professor of chemistry at the University of Berlin, whose name will live forever by his Reagent of Phosphomolybdic Acid as a precipitant of alkaloids, publishes his "Handbuch der analytischen Chemie."

W. H. Kolbe (1817-1884), famous for the constitution and synthesis of salicylic acid, founded the *Journal für praktische Chemie*.

*Pharmazeutischer Zentralanzeiger*, the official organ of the German drug clerks, is established.

A. Oppenheim translates into German "Historie des doctrines chimiques depuis Lavoisier jusqu'à nos jours," by Prof. Charles A. Wurtz, of Paris, which contains the sentence "La chimie est une science Française," thus giving rise to many arguments by chemists in the Fatherland, who added the slogan, "But chemistry was developed in Germany."

#### BORN IN 1870.

My list of pharmacists born in that year is rather small.

Nicolas Klein, of Louisville, Ky., born January 9, 1870, was apprenticed to Theo. Ractanus. He died December 29, 1907.

Wm. J. McAdams, of Pittsburg, Pa., born in 1870, and died in 1910.

The author would be pleased to receive short biographies of pharmacists born since 1870, to be incorporated in his historical notes.

## DIED IN 1870.

## OTTO.

Friedrich Julius Otto, born January 8, 1809, in Grossenhain, Germany, was an apotheker, then teacher, and in 1833 professor at the Collegium Carolinum, Braunschweig, until his death on January 12, 1870. In 1840 he translated Graham's Elements and in 1854 he enlarged same into a master work "Ausführliches Lehrbuch der Chemie." In 1856 he published, together with his son, Dr. Robert Otto, of the University of Greifswald, the classic work "Auleitung zur Ausmittlung der Gifte" and thus became one of the pioneers in legal chemical analysis. He modified and improved the method of the Belgian chemist, Jean Servais Stas, so that the Stas-Otto process of the detection of individual alkaloids is still considered authoritative to-day. He was also a collaborator on Bolley's "Handbuch der Technologie."

## BOLLEY.

Pompeius Alexander Bolley, born May 7, 1812, in Heidelberg, since 1838 professor in Arau and since 1855 at the polytechnicum in Zurich, Switzerland, until his death, August 3, 1870. In 1852 he published his classic work "Handbuch der technisch-chemischen Untersuchungen." Bolley is also the father of the renowned work in 8 volumes "Handbuch der Chemischen Technologie" (Braunschweig, 1862), in which celebrated scientists of the times were collaborators. He was an authority on coloring substances and in 1868 published "Altes und Neues ans der Farbenchemie." His many researches and those of the students in his laboratory are published in *Annalen Chemie und Pharmacie* and in *Schweizerische polytechnische Zeitschrift*.

## EHRMANN.

Martin J. Ehrmann, born 1809, was professor of pharmacy in Brünn and later in Vienna. He wrote a commentary on the Austrian Pharmacopoeia in four volumes. "Lehrbuch der Pharmazie nachdem gegenwarligen Staudihrer Gumdwissusschaften," Vienna, 1826-28 and 1832-33. In 1847 he founded the *Oesterreichische Zeitschrift für Pharmazie*. He died in 1870.



REDTENBACHER.

Joseph Redtenbacher was born in 1810 at Kirchdorf, Austria. He advanced to professor of chemistry and attained fame through his work on glycerin and the preparation of oenanthylic or heptical acid,  $C_6H_{11}COOH$ , by the oxidation of oleic acid with nitric acid. Redtenbacher died in 1870.

BLASIUS.

Johann Heinrich Blasius was born, October 8, 1908, in Eckerbach, near Cologne. After being a school teacher in Krefeld he became, in 1836, Professor of Natural Sciences at the Carolina University, Braunschweig. Here he was also director of the Botanic Gardens and the Museum of Natural History. He died May 27, 1870.

MAGNUS.

Henrich Gustav Magnus, celebrated chemist and physicist, born in Berlin, May 2, 1802, studied in his home city and Paris and also under Berzelius in Stockholm. In 1831 he became teacher, in 1834 extraordinary professor, and in 1845 professor of physics and technology at the University of Berlin. In 1869 he retired and died April 5, 1870.

Magnus enriched Physics and Chemistry with many important researches. He determined the coefficient of expansion of several gases, the tension of vapors, the density of ice at different temperatures. His papers dealing with electricity, magnetism and hydraulics are published mostly in Poggendorff's *Annalen*.

Although not pharmacists or chemists, the following four members of the medical profession deserve to be remembered here.

SYME.

James Syme (1799-1870) of Edinburg, was a cousin of the celebrated Dr. Robert Liston. He succeeded the latter in his very large Scotch practice as well as his professorship. In clinical surgery his name continues to live by the amputation of the ankle-joint, known as Syme's Amputation. With Simpson and Pirogoff he was the first European surgeon to adopt, in 1847, ether anesthesia. In 1868 he was also the first to welcome the antiseptic method of his best and greatest pupil and his son-in-law, Lord Lister.

## COPELAND.

Dr. James Copeland (1891-1970), of the Orkney Islands, was a medical polyhistorian. His Dictionary of Practical Medicine (1834-59) contains 3509 double column pages, all written by himself. As president of the Pathological Society of London, Copeland excited many a chuckle of derision when he claimed various modern discoveries as his own.

## GRAEFE.

Albrecht von Graefe (1821-1870), of Berlin, was the creator of the modern surgery of the eye, in fact the greatest of all eye surgeons. In 1854 he founded the Archiv. für Ophthalmologie, the leading organ of this special branch of medicine to date. Graefe's clinic became famous all over the world and not only student but practising physicians came to Berlin to study ophthalmology under its greatest master.

## SIMPSON.

Although not a pharmacist, but a physician, I must not forget to record the death of Sir James Young Simpson, because he introduced chloroform as an anesthetic. Born in 1811 in Linlithgow, Scotland, as the son of a baker, it was the desire of his parents to have him educated. In 1825 he entered the University of Edinburgh, studied hard, and in 1832, at the age of twenty-one, he graduated as M.D. His thesis, "On death from Inflammation," so impressed the professor of Pathology that he selected the recent graduate as his assistant. In 1840 Simpson became professor of Obstetrics and through his great ability and fascinating personality soon acquired an enormous practice.

The following short account of the introduction of chloroform as an anesthetic is taken from the author's lectures and might be of interest at this time.

Not being quite satisfied with the effects of ether, which he was the first to employ in obstetric cases, namely January 19, 1847, Simpson searched for a more lasting anesthetic. He tried many substances, liquids, solids and gases, but without success. A Scotch pharmacist, David Waldie, at that time manager of the Liverpool Apothecaries Company, visited Edinburgh during the summer of 1847 and advised Simpson to try chloroform, promised to send some on his return to Liverpool. However, a fire in the laboratory of his

establishment prevented the fulfillment of this promise. Simpson then obtained a bottle of chloroform from Duncan and Flockhart, in Edinburgh, but owing to its specific gravity, did not consider it of much value. How could such a heavy liquid act as an anesthetic? In the evening of November 4, 1847, a date worth remembering, Prof. Simpson and his two talented assistants, Drs. Duncan and Keith, tried chloroform by inhaling it from tumblers. The effect was instantaneous and remarkable. Dr. Keith's eyes grew bright and he laughed heartily. Dr. Duncan waltzed around the room and Dr. Simpson, the dignified professor of Medicine and Midwifery at the University of Edinburgh, wiggled his toes and would have stood on his learned head for a doughnut. When some ladies entered the room, the three gentlemen were remarkably amiable, loquacious and even hilarious. Little did they dream that these gay Lotharies were drunk—drunk on chloroform. Then the secondary effects of the chloroform vapors became evident, the charming doctors became confused and then unconscious. Simpson was the first to revive. He found Duncan under the table with eyes staring and snoring loudly, while Keith was kicking at the supper table. The experiment was repeated a few evenings later, and this time Miss Petrie, a niece of Simpson, wanted to prove that she was as brave as a man, inhaled the chloroform. She folded her arms across her breast and fell asleep murmuring, "I am an angel! Oh, I'm an angel"—but Simpson searched in vain for her wings. "Better than ether," was Simpson's conclusion. He read a paper on Anaesthetics before the Medico-Chirurgical Society of Edinburgh, calling attention to the superiority of chloroform over ether, and he also began at once to use it in his obstetrical practice and with great success.

Strange as it may seem, all innovations meet with strenuous opposition. And so it was with the introduction of chloroform as an anesthetic in obstetrics. Not only the unscientific rabble shouted at Simpson, but also men of brains and skill opposed the innovation, as Meigs, of Philadelphia, Ramsbotham, of Great Britain, and Scanzoni, of Germany. Even the church opposed this apparent blessing and the orthodox quoted the passage in Genesis III, 16: "In sorrow thou shalt bring forth children." The controversy grew so bitter that had Simpson been a Semmelweis he might have become insane, and had he been a Horace Wells he would have killed himself. But he was the right man in the right place. He had the

courage which defends and the courage which attacks. He was the leader of a great battle and he fought it with a clenched fist. He answered Scripture by Scripture and quoted Genesis II, 21, in which it is related that when the Lord wished to take a rib from Adam in order to make Eve, "God caused a deep sleep to fall upon Adam and he slept." Thus it was proven that God himself made use of anesthetics in difficult operations.

When Queen Victoria herself, on two occasions, availed herself of chloroform as an anesthetic in obstetrics and administered by Simpson himself, then the heretic became a hero, the rebel became a savior: In due time the baker's son had a Sir in front of his name and a Bart. after. The doctor adopted for his coat of arms the rod of Aesculapius over the motto *Victo dolere!* Oxford gave him a D.C.L., Edinburgh has his statute, and his bust stands in Westminster Abbey.

Although not strictly pharmaceutical, I want to record briefly the death of two literary authorities.

#### DUMAS.

Alexander Dumas (Père) was born in 1802 near Dieppe, the son of one of Napoleon's generals, a Haytian mulatto of ability and education. Dumas became the Walter Scott of France with a succession of historical works which have been the delight of three generations. He died in 1870.

#### DICKENS.

Charles Dickens, one of the greatest of English novelists, was born in 1812. His "Pickwick Papers" in 1836 won him fame and wealth. His keen description, human pathos, knowledge of child nature, comedy, tragedy and romance, appealing to the average mind, made Dickens one of the most influential writers of the 19th century. He died in 1870.

#### CONCLUSIONS.

If this paper arouses a little more interest in that much neglected subject, history of pharmacy, the writer is well paid for the trouble he has taken. The sooner the pharmacist will realize that even a little knowledge of history will benefit him, intellectually and also financially, the better will it be for professional pharmacy.

In case the members of the New Jersey Pharmaceutical Association appreciate these historical notes, the author is perfectly willing to promise annually a paper on "Pharmaceutical Events Fifty Years Ago."

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## COLLOIDAL PREPARATIONS IN MEDICINE.

The June number of *The Prescriber* is devoted almost entirely to a presentation of the use of colloids in medicine. The importance of the subject and likewise the excellence of its treatment leads us to present to our readers copious abstracts from the articles appearing in this esteemed medical cotemporary.

**COLLOIDS IN GENERAL PRACTICE.**—Under this caption editorial comment is made. Colloid therapy is not only new—it is still very markedly in the experimental stage. The preparation of colloids is, in many instances, no very difficult matter: the difficulty begins in the attempt to make them therapeutically valuable. The general practitioner should satisfy himself that he is using colloids of the right strength, whose therapeutic properties are sufficiently known, which are suitable for internal administration, orally or by intravenous injection.

Speaking generally, a colloid is a solution of some "insoluble" substance—generally an element. For example, colloid silver is a clear red liquid. It passes through a filter and, to all simple tests, answers as would any other solution. The colloid solution referred to is unstable and readily desposits silver as a precipitate. When this occurs it is, of course, colloidal no longer, and any value it possesses as a colloid disappears. It is this precipitation, this disappearance of the colloid as such, which has to be in some way obviated before any colloidal preparation can be of the smallest use in medicine.

The importance of colloids in medicine arises from the fact that most, perhaps all, the fluids of the body are colloidal in character. It is not then to be wondered at that some astonishing results have been obtained from the use of colloids. In many cases it would seem as if, in this way, all the advantages, and none of the drawbacks of the particular drug used, were embodied in the colloidal state. Thus colloidal mercury may be given wherever mercury is indicated; it is only feebly toxic and it is very rapidly absorbed—two striking advantages over the salts of mercury. Similarly colloidal sulphur would appear to be the best possible form for the administration of that element. Ordinary sulphur is not absorbed either in the stomach or elsewhere, whereas colloidal sulphur combines with protein, is rapidly absorbed and is carried to those parts which need it. Again, no colloid has been used with greater suc-

cess than that of silver. The results obtained from the use of collosol manganese have likewise been little short of astonishing. Colloidal iron is of great use in treating anaemia and chlorosis. An interesting fact is that it unites with the amino-acids of the stomach, forming a compound from which haemoglobin is synthesized in the system. Colloidal iodine has been in use for some time and is tolerably well known to the practitioner.

Lastly, it is clearly to be borne in mind that colloidal preparations are not to be relied upon unless they are fresh. As we said above, the colloidal state is essentially unstable; the substance in the form of a colloid is precipitated by the particles of salt which abound in the atmosphere, and even by the minute quantities of matter dissolved from the containing vessel, as well as by forces at present not clearly apprehended.

COLLOIDS AS ANTISEPTICS.—This is another topic editorially commented upon. There is one other property possessed by colloids, however, which is of direct medical interest—their use as antiseptics or germicides. Bacteria, physically considered, are colloidal in character, as are the fluids in which their life-cycle is passed. All colloids—or rather the particles in colloid solution—are electrically charged, either positively or negatively as the case may be. Most substances bear the same charge always, though there are some colloids which, if prepared in one way, are negatively charged, and if prepared in an alternative way, are positively charged. Bacteria are negatively charged, hence, if in any way it is possible to neutralize this electric charge the bacteria are precipitated, and are thus removed from the sphere of deleterious action. The obvious way to neutralize (electrically) a negative sol is to add, in proper proportion, a positive sol. One can thus imagine the power of, and the convenience of using, an antiseptic which has the following properties—that of precipitating bacteria, that of being chemically a germicide, and that of being non-toxic and non-caustic. Such would be the properties of the ideal antiseptic, and such are the properties of certain colloids—those, namely, which bear a positive charge and which are also antiseptic by reason of their chemical properties.

The most valuable colloid by far, in this connection, is colloidal silver. It has approximately the same germicidal action as mercuric chloride, and in addition it is non-toxic, non-caustic, and non-irritating. It has the curious property, when injected intravenously,

of rendering rabbits immune from anthrax and diphtheria bacilli. Again, colloidal silver is interesting in that it has a selective germicidal action upon the pneumococcus and the micrococcus catarrhalis.

The following fact, germane to the present subject, is also of great interest: The progress of any ailment of bacterial origin depends in large measure upon the physical (electric) conditions of the body fluids in which the bacteria reproduce themselves. It is possible so to change these fluids (which we repeat are invariably colloidal) by the injection of colloids prepared in the laboratory that the development of the bacteria is hampered and the progress of the disease checked. Here then is a new method of treating contagious and infectious diseases. Instead of, or supplementary to, vaccines, serums, or ordinary drugs, there is suggested the use of certain colloids which so act upon the "soil" in which the bacteria grow that the latter fail to develop. This branch of colloid therapy is as yet in its early infancy, but it needs no leap of the imagination to picture the possibilities which may be unfolded by research.

**COLLOIDAL METALS AND NON-METALS: THEIR HISTORY, PREPARATION, AND PROPERTIES.**—Thos. Stephenson contributes a résumé under this title. The first publication in English literature concerning the use of this class of medicines is stated to have appeared in September, 1907. Graham first used the word "colloid" to distinguish certain amorphous substances, of which glue and gelatin are typical examples, which diffuse with difficult through membranes, as opposed to "crystalloids," which diffuse with ease. The word is now used to describe a condition which chemical substances may be made to assume rather than to define a definite class of compounds. A "colloidal solution," or "sol," is not a solution in the strict sense of the term, but rather a suspension of minute particles of the substance.

The nature and properties of colloids and of colloidal sols have been known for some time, but the assumption by the metals and metalloids of the colloidal state is a comparatively recent discovery. It is these that have come into extensive use in medicine. The first metal to be used in this way was colloidal silver, which was introduced in 1896 under the name "collargol." Collargol is sold in the form of small black scales having a metallic luster forming with water an opaque solution. It is not really a colloidal metal but is considered as a combination of an acid silver molecule with ammonia, *i. e.*, collargolate of ammonia.

Shortly after the introduction of collargol, Trillet succeeded in preparing derivatives of certain metals by precipitating solutions of metallic salts with an alkali in presence of albumin, forming a kind of colloidal sols of the metals. Later, Bredig produced true colloidal "sols" of the metals by passing an electric current through pure water between electrodes of the metal to be dissolved. The current diffuses a minute quantity of the metal throughout the liquid—the metal, in fact, becomes volatilized in the liquid. The resulting sol is in every case a dichroic liquid, transparent to transmitted light and opaque to reflected light. The suspended particles in a properly prepared Bredig colloidal sol are so minute that they can be detected only by the ultra-microscope, and they possess the vibratory motion known as "Brownian movement."

The early literature concerning the therapeutic action of these liquids was practically confined to France. A. Robin was the pioneer student in this field. He compared the sols of Bredig first to organic enzymes and then later to antitoxic serums. He is enthusiastic as to their possibilities and describes wonderful effects obtained from them in the treatment of pneumonia, articular rheumatism, puerperal infections, meningitis, etc. The great difficulty attending the use of electrically prepared colloidal metals was their unstableness. The particles had a natural tendency to agglutinate and in consequence the solution did not remain therapeutically active for more than a few hours. Sterilization by heat caused the particles to agglutinate and the same result followed the addition of a foreign substance such as sodium chloride. When injected into the blood, the colloidal sol at once agglutinated and any therapeutic action was consequently nullified. It was found that the introduction of a small portion of another colloid such as gelatin or gum, at a suitable stage in the manufacture, prevented this agglutination and the addition of such a substance known as a "protective colloid" has allowed of these preparations being preserved and isotonized, and this discovery made colloidal metals a commercial as well as a therapeutic possibility.

Electrically prepared colloidal sols are not stable enough for therapeutic purposes, so that the methods now generally employed are chemical ones and in the case of a metallic colloid consist in the reduction of the metallic salt by a suitable agent in the presence of a protective colloid such as gelatin or gum. The metal is produced in a very fine state of subdivision and is kept in this condition by the protective colloid, the by-products are removed by dialysis.



Under the name of "organosols" Martindale describes colloidal metals obtained by impregnation of lanolin with an aqueous solution of the salt of a metal and subsequent trituration with a solution of alkali hydroxide. By double decomposition the oxides or hydroxides of the heavy metals may thus be obtained as colloids, and the product may be dissolved in ether, fats, or in liquid paraffin, the cholesterol acting as the protective agent.

Colloidal sulphur may be prepared by mixing solutions of sodium sulphide and sodium sulphite, adding white of egg and stirring thoroughly; lastly adding dilute hydrochloric acid and dialyzing. Colloidal iodine may be obtained in several forms: aqueous, oil and ointment. Colloidal alkaloids have also been prepared, but their use so far has not become general. Colloidal quinine, curiously enough, has no action in malaria.

Colloidal antimony sulphide is prepared from a solution of tartar emetic with sulphuretted hydrogen. The potassium bitartrate formed is removed by dialysis and glucose is added to make the solution isotonic, gum acacia as a protective, and phenol as a preservative.

For a time it was thought that the therapeutic action of colloidal sols was merely catalytic or mechanical, but it is now believed that other factors are responsible. The results recorded for several of these all point to an intensification of the specific action of the metal, which is probably in the ionic condition. The fact remains that whereas it was originally thought—and, probably, with some reason in the case of Bredig's solutions—that the actual metal was immaterial, it is now known that the different colloidal metals have different therapeutic effects, and cannot be employed indiscriminately.

There is undoubtedly a great future for colloidal remedies and we are now only standing on the threshold of what may be learned about them. Improved methods of preparation will enable fresh colloidal sols to be prepared and will lead to the discovery of fresh fields for their employment and additional laurels for the therapist.

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#### THE END OF SIMPLIFIED SPELLING.\*

There no doubt has been some surprise, but probably little expressed regret, because of the recent announcement, made by the Modern Language Association of America, that it has withdrawn its sanction of the simplified spelling movement. The reason given,

\* From *Montreal Pharmaceutical Journal*, April, 1920.

while not necessarily sufficiently conclusive to warrant the abandonment of a campaign long and vigorously conducted, may, after all, seem to be so. These are the lack of public interest in the proposed new form of spelling, its failure to make any appreciable progress, and its offensiveness to some members of the association. The movement to reform English spelling in the United States took definite shape in the year 1906, when the Simplified Spelling Board was organized in New York City. Many distinguished men and women have, at one time and another, been identified with the campaign, and from the first it was liberally financed. Reams of literature in the form of more or less convincing propaganda, have been printed and distributed throughout the length and breadth of the land, the chief effort, especially early in the campaign, being made to win over the support of colleges and universities through appeals made to their executives or to those employed as professors or instructors. The board published, not long after its organization, a list of 825 American college professors and officers who, it was claimed, had agreed to follow the prescribed simplified form of spelling in the use of 300 words, wherever possible. Further impetus was given to the movement, momentarily at least, in August, 1906, when Theodore Roosevelt, then President of the United States, ordered the public printer to adopt the spelling advocated by the board in the publication of all documents of the executive departments. Due to public protests, this order was modified, a little later, to apply only to the official correspondence of the White House.

It might, perhaps, have been supposed that a movement so thoroughly organized, so liberally financed, and quite generally indorsed by educators in some parts of the country, especially as it had the support and approval of the editors of a number of the more popular dictionaries, must eventually succeed. But the fact remains that it did not succeed. Indeed, it never even approached success. The popular protest which reached President Roosevelt seemed to express the almost unanimous sentiment of the masses. Those who opposed arbitrary innovations along the lines proposed insisted, and apparently with reason, that spelling reform should continue to be, as it always had been, a matter of growth. Those persons who had learned to spell the words in common use quite emphatically insisted upon the right to continue the spellings they had learned. They admitted that many of these spellings were arbitrary, in a sense, but that they were no more arbitrary than the so-called simplified forms prescribed,

and that no method of phonetic spelling could ever be successfully standardized. Perhaps many of the sticklers for the older form may have admitted that there were many words, some of them in quite common use, which they knew "by sight" only, and with which they had no "speaking acquaintance," but they evinced no inordinate desire to be compelled to form unnumbered new acquaintances, as it were, the presentations to be made by writers who claimed the privilege of disguising and camouflaging the English language to suit their own whims.

There is, of course, a trend toward what all admit to be, or claim to be, a "modern" form of spelling. Even a cursory examination of the accepted forms in use to-day would be convincing of the accuracy of this statement. But it might be quite difficult to bring convincing argument that the changes involved had ever been arbitrarily made. Tennyson and Swinburne employed, in the spelling of many words, forms quite different from those followed by Shakespeare and Bacon, and, no doubt to those earlier writers the forms employed by Wyclif appeared antiquated, if not grotesque. The change from one form to another has been gradual and almost unnoticed, as are the changes to which all become accustomed in dress, and even in so-called correct forms of etiquette. There is evidently no need to tell a people that its language is indefensible etymologically as well as on grounds of accepted usage. But it has been proved apparently, that its merit of familiarity is its sufficient defense.

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## THE SELECTION OF GLASS FOR THE MANUFACTURE OF AMPULS.\*

BY GEORGE E. ÉWE,

CHIEF CHEMIST, H. K. MULFORD COMPANY, PHILADELPHIA.

The selection of and requirements for glass bottles for storing the ordinary elixirs, fluidextracts, powders, tablets, etc., employed in pharmacy is a crude process, indeed, in comparison with the careful tests required for the selection of a proper glass for the manufacture of ampuls. This care is necessitated by reason of the fact that unselected glass may possess sufficient free alkali, or may be capable of yielding sufficient free alkali under the stress of the

\* From *Jour. Franklin Institute*, May, 1920.

sterilization process which ampul solutions are required to undergo, or may yield sufficient alkali in the period during which they are necessarily kept in stock before being sold, to cause the precipitation of a portion of the alkaloidal base of a solution of alkaloidal salt when placed in the ampuls, and because unselected glass may throw off spicules or splinters of glass under the stress of the sterilization process or during storage. It is sufficient merely to point out, in order to show the unsuitability and even danger in the use of improperly selected glass, that precipitation of alkaloidal base will result in the lowering of the efficacy of an ampul solution upon which a physician may be relying in a serious case of illness and the production of spicules or splinters of glass in the ampul solution may result in discomfort, local irritation, or possibly more remote and more dangerous consequences. The use of a slight addition of acid to ampul solutions in an effort to correct for the alkalinity of unselected or improperly selected glass is contra-indicated in view of the fact that glass can be made or selected which requires no use of acid. The use of acid is also contra-indicated because acidity is usually productive of irritation at the site of injection.

In outlining tests for the selection of glass for the manufacture of ampuls the working of the glass under the flame must also be considered. In addition, other tests which may act as checks on the "alkalinity," "spicule" and "flame" tests are frequently resorted to. The series of tests mentioned below will, as a rule, be sufficient for proper selection of glass, if applied "*secundum artae*." However, the "art," particularly the "flame" testing can be attained only by practical experience.

#### TESTS FOR THE SELECTION OF GLASS FOR THE MANUFACTURE OF AMPULS.

*Size of tubing, thickness of wall, freedom from certain proscribed ingredients, color:* in accordance with specifications.

"*Working under the flame:*" can be judged only by practical experience obtained by comparison of many varieties of glass.

*Standard:* greatest ease in working consistent with the other requirements.

"*Alkaloidal Alkalinity Test*"—"General."—A 1 per cent. solution of U. S. P. morphine sulphate or a 0.2 per cent. solution of U. S. P. strychnine sulphate in normal saline solution must not develop crystals or become turbid or opalescent when sterilized under prac-

tical conditions in ampuls made from the glass undergoing test; the ampuls having been treated with dilute hydrochloric acid and finally thoroughly washed free from acid and dried before the alkaloidal solution is placed in them. The preferred test is the "particular" one which is in all respects similar to the "general" test except that the particular solution which is intended to be marketed in the ampuls is used in place of the morphine sulphate or strychnine sulphate solutions.

"*Spicule Test.*"—Work the glass into ampuls. Place a 0.6 per cent. NaCl solution (or any particular solution) in the ampuls; seal and sterilize under practical conditions. The solution is then carefully examined under a magnifying glass for spicules or splinters of glass.

Exact conformity with the above test is absolutely necessary in order to permit the use of any particular glass for the manufacture of ampuls.

The following tests are applicable for comparative purposes only, and are occasionally employed as confirmatory checks:

"*Phenolphthalein Alkalinity Test.*"—Treat the glass with dilute HCl followed by very thorough washing. Boil a sample corresponding to 500 sq. centimeters of surface for 16 hours with distilled water, keeping the sample covered with fresh additions of water as required. Remove the glass, add 1 Cc. phenolphthalein test solution to the water in which the glass was boiled and titrate to neutrality. Make a correction on the water, vessel in which the boiling was conducted, locality in which the test was carried out, etc., by running a blank under precisely the same conditions employed in making the test, and at the same time. Report alkalinity as milligrams of NaOH per 100 sq. cm.

"*Loss to Water Test.*"—The sample used in the "phenolphthalein alkalinity test" is weighed before and after boiling. Report loss as milligrams per 100 sq. cm.

"*Vulnerability to Alkaline Fluids Test.*"—Repeat the "loss to water test," using a new sample, and using 2 per cent. sodium carbonate solution in place of water, keeping up the volume by fresh additions of water only. Report loss as milligrams per 100 sq. cm.

"*Phenolphthalein Alkalinity Autoclave Test.*"—Water containing a few drops of phenolphthalein test solution is placed in the ampul which has previously been acid-washed and thoroughly rinsed with distilled water); the ampul is sealed and autoclaved at 12 lbs. steam

pressure for 45 minutes. At the end of this time the tube is carefully examined for color and spicules. A pink color indicates alkalinity.

"*Phenolsulphonephthalein Alkalinity Autoclave Test.*"—In all respects this is similar to the preceding test with the exception that a yellowish solution of phenolsulphonephthalein is used instead of phenolphthalein and the autoclaved liquid is examined for any reddish tint which may develop.

The following table shows some typical results obtained by the use of the several tests mentioned above in glass tubing offered for the manufacture of ampuls:

Sample No.	Color.	"Flame" test.	"Spicule" test.	"Phenolphthalein Alkalinity" test.	"Loss to Water" test.	Suitability.
1	Flint	O. K.	None	0.098 Mgm.	0.7 Mgm.	O. K.
2	Flint	Works hard	Spicules	.....	4.2 Mgm.	Not O. K.
3	Flint	Works easily	Spicules	.....	1.9 Mgm.	Not O. K.
4	Flint	Works easily	None	Undeter. trace	0.61 Mgm.	O. K.
5	Flint	Works easily	None	0.102 Mgm.	1.1 Mgm.	O. K.
6	Flint	Works hard	Spicules	.....	Unweigh- able	Not O. K.
7	Flint	Works easily	None	.....	0.62 Mgm.	O. K.
8	Flint	Works easily	None	.....	0.49 Mgm.	O. K.
9	Flint	Works easily	None	.....	3.2 Mgm.	O. K.
10	Flint	Works easily	A few spic- ules	.....	4.4 Mgm.	Not O. K.

All of these samples yielded perfect results in the "alkaloidal alkalinity" test. As a matter of fact, after a satisfactory source has been established, it is only occasionally that a sample fails to answer this requirement, but this occasional exception illustrates the necessity for the application of this test.

The relation between the alkalinity yielded in the "phenolphthalein alkalinity" test and the result of the "alkaloidal alkalinity" test was not determined, the "phenolphthalein alkalinity" test being rejected in favor of the shorter and more practical "alkaloidal alkalinity" test.

The phenolphthalein and phenolsulphonephthalein alkalinity autoclave tests are used by some workers, but they are open to the criticism that they bear no practical direct relation to the possible use of the glass for ampul purposes, whereas in the same time and with no more labor a direct result can be obtained by the use of the "alkaloidal alkalinity" test.

The results yielded by the application of the "phenolphthalein alkalinity," "loss to water" and "vulnerability to alkaline fluids" tests to some samples of glass tubing, bottles, Erlenmeyer flasks, test tubes and beakers are herewith appended as a matter of comparison and of interest:

Sample.	Color.	"Phenolphthalein Alkalinity" test.	"Loss to Water" test.	"Vulnerability to Alkaline Fluids" test.
Tubing	Flint	Undeterminable trace	Unweighable	21.0 Mgm.
Tubing	Flint	.....	1.5 Mgm.	....
Tubing	Flint	Undeterminable trace	Unweighable	30.0 Mgm.
Tubing	Flint	.....	1.17 Mgm.	....
Tubing	Flint	Undeterminable trace	Unweighable	24 Mgm.
Tubing	Flint	Undeterminable trace	Unweighable	8.25 Mgm.
Tubing	Flint	.....	1.2 Mgm.	....
Tubing	Flint	.....	4.0 Mgm.	22.5 Mgm.
Tubing	Flint	.....	2.5 Mgm.	43.5 Mgm.
Tubing	Flint	.....	0.62 Mgm.	....
Tubing	Flint	.....	2.5 Mgm.	31.5 Mgm.
Tubing	Flint	.....	3.0 Mgm.	27.5 Mgm.
Tubing	Flint	.....	3.1 Mgm.	....
Tubing	Flint	.....	3.5 Mgm.	24.0 Mgm.
Tubing	Flint	.....	Unweighable	9.25 Mgm.
Tubing	Flint	Undeterminable trace	Unweighable	6.5 Mgm.
Tubing	Flint	.....	Unweighable	20.0 Mgm.
Tubing	Flint	.....	Unweighable	17.5 Mgm.
Tubing	Amber	.....	Unweighable	2.65 Mgm.
Tubing	Amber	.....	Unweighable	2.0 Mgm.
Tubing	Amber	.....	8.0 Mgm.	56.5 Mgm.
Tubing	Amber	.....	1.5 Mgm.	22.5 Mgm.
Tubing	Amber	.....	3.0 Mgm.	27.5 Mgm.
Tubing	Amber	.....	4.0 Mgm.	19.0 Mgm.
Tubing	Amber	.....	5.0 Mgm.	12.5 Mgm.
Tubing	Amber	.....	8.0 Mgm.	25.0 Mgm.
Tubing	Amber	.....	10.0 Mgm.	57.5 Mgm.
Tubing	Amber	.....	Unweighable	7.5 Mgm.
Tubing	Amber	.....	Unweighable	7.8 Mgm.
Tubing	Blue	.....	0.15 Mgm.	1.8 Mgm.
Bottle	Flint	.....	0.45 Mgm.	....
Bottle	Flint	.....	0.59 Mgm.	....
Bottle	Flint	.....	0.39 Mgm.	....
Erlenmeyer flask	Flint	.....	0.0107 Mgm.	....
Test tubes	Flint	Undeterminable trace	0.28 Mgm.	....
Beaker	Flint	Undeterminable trace	3.0 Mgm.	....
Beaker	Flint	.....	Unweighable	3.3 Mgm.
Beaker	Flint	Undeterminable trace	Unweighable	18.5 Mgm.
Beaker	Flint	Undeterminable trace	Unweighable	13.0 Mgm.

No definite information can be obtained regarding the possible formation of spicules by a glass, from its working qualities under the flame. In the experience of some workers, the hard glasses appear to suffer surface scaling under the influence of the moisture and heat used in autoclaving, whereas in the experience of others, the more easily worked and more soluble glasses yield spicules by surface erosion due to solution of the alkaline radicle of the glass.

PHARMACEUTICAL RESEARCH LABORATORY,  
H. K. MULFORD COMPANY.

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## ECONOMIC BOTANY AND CHEMICAL INDUSTRY.\*

BY J. B. FARMER.

The events of the last few years have served to emphasize the need of looking more fully than heretofore into the best means of utilizing vegetable products as raw materials for industry, or of investigating their amenability to chemical treatment. We are mainly dependent upon plants for the great sources of our material wealth, and, indeed, plants (and in a secondary sense animals also) represent the main real revenue of the world, inasmuch as they are practically the chief storers of the energy that reaches us from the sun.

Few people sufficiently visualize our absolute dependence on the plants for the sheer necessities of life, or realize how urgent is the demand for investigations which will enable us not only to increase our wealth, but also give us a further measure of control over the sources of, and the conditions that affect, this plant revenue. The need for such investigation begins at the bottom. We have much need for stocktaking. At home there is, for example, a problem why some grass fields will fatten stock, and others not. Such fields are known in most grazing districts, but no really satisfactory explanation of their excellence is forthcoming. Superficial reasons, so-called, are common enough, but the fact that such fields are often surrounded by others apparently similar but of greatly inferior value should give pause enough to those who are ready with facile solutions of a difficult problem—or, rather, congeries of problems. Indeed, the soil and the grass that grows on it still constitute a relatively open field of research. Chemical analyses of soil go a

\*From *Jour. Soc. Chem. Industry*, May 15, 1920.



little, but only a little, way. The complex physical and physico-chemical conditions and the relation of the plant roots to the substratum, and the changes that may be induced in the herbage itself, are very little understood; indeed, it would be almost true to say that the real problems have as yet scarcely been formulated. Hall and Russell in this country have emphasized the importance of the physical texture of the land. Russell and his collaborators at Rothamsted have done first-rate pioneer work in investigating the importance of the inter-relations of protozoa and bacteria in connection with soil fertility, and during the last three or four decades we have come to recognize that the problems of fertility are not likely to be elucidated by the older test-tube chemistry. They demand for their analysis chemists with a biological training and outlook, as well as biologists with a corresponding equipment in chemistry and physics. At present the two branches of science are often undesirably divorced although, largely owing to pestilent systems of examinations, a lack of biological training among chemists is far more common than is a corresponding ignorance of "physical" science with biologists, at any rate those on the physiological side. It is not, of course, suggested that every student should attempt to *specialize* in both of these great branches of science, but it is certainly a bar to progress that a student of the one should continue to be entirely ignorant of the more fundamental principles of the other. Those who are cognisant of the facts will be able of their own knowledge to supply examples enough during the late war—examples that would have been humorous, had the consequences not been fraught with too much gravity at the time.

One of the happier developments arising out of the war consists in the greatly increased recognition in this country of the value of science to industrial enterprise, and this is becoming as prominent in the biological as in the chemical and engineering worlds. Botany in its various branches is in a position to render very important services at the present time, and the supply of properly trained young men is as yet quite inadequate to take advantage of the new situation that has arisen. The exploitation of oil, rubber and other tropical products, the fermentation industries—indeed, all connected with the utilization of plants and plant products, afford large and profitable scope for scientifically directed industrialism. It is the business of the botanist not merely to find the raw material, but to improve it by careful breeding, to defend it from the attacks of

enemies, both animal and vegetable, and to investigate the conditions under which the yield of the desired product can be improved, whether by appropriate modification of the environment or by breeding. As the nature of the problems becomes more clearly recognized the methods of cultivation, selection and dealing with the raw material improve. Breeding, which used to be a sort of hit-and-miss business, is now becoming more and more an exact science, and although, owing to the tangled mass of factors involved, immediate success in a particular direction cannot always be predicted, at any rate we do not know how to attack the matter. Thus it is that in the more direct cases it is now possible with comparative certainty and rapidity to achieve results which formerly could only be secured by an immense waste of time, material and, of course, expense. Intelligent breeding demands a wide outlook over the many aspects presented by any single organism, but this fact is still unappreciated by too many business men. To give but one example, one often hears of high expectations being entertained that races of rubber trees can easily be produced which shall give high yields of caoutchouc, shall be immune to the attacks of disease, and, in short, shall possess all sorts of desirable qualities that, unfortunately, are but seldom combined in a single individual. Such expectations are entirely unreasonable, at any rate for so long as we continue to remain ignorant of the physiological significance of latex in the tree, of the origin and significance of caoutchouc formation, as well as of the other substances that occur along with it. Possibly it may turn out that there exists a significant connection between the caoutchouc and the troublesome resin which seems invariably to accompany it in all rubber yielding latices. The destiny of the oxygen during the transformation from carbohydrates to rubber is in itself an attractive, and perhaps a very fundamental, problem.

The matter of immunity to fungal and other disease-producing organisms is of the widest possible interest. In our own cultivated crops the problem is ever arising. Why do *Victoria* plums suffer so badly from silver leaf (due to the fungus *Stereum*), and why do certain otherwise desirable varieties of potatoes fall victims to the attack of wart disease so that they cannot be grown at all in districts where the disease is present? It is plain that there is joint work here for the plant physiologist and the chemist. There will have to be "many knots unravelled by the road" before the secrets of

immunity are disclosed, and even if the final goal be distant the knowledge gained on the way thereto cannot fail to be very productive in all sorts of ways as yet entirely unsuspected.

Fortunately, however, there are many problems of far more simple type, some of which are being solved, and others seem ripe for solution. For example, both in the field and in the laboratory the amount of scientific work that is urgently needed in connection with cotton is stupendous, and the results will have an imperial no less than a national influence and significance.

The vast sums of money which the great cotton industry is setting aside for scientific research is proof enough that the leaders are alive to the issues at stake. It is with special pleasure that reference is here made to the prize offered by Messrs. Cross and Bevan for an essay on "The interconnection of Economic Botany and Chemical Industry." In the pages of this JOURNAL it would be superfluous to dwell on the advances in our knowledge of cellulose and its products which we owe to these investigators, but what they have done for cellulose can be repeated by others for many other raw products, to the great advantage of commerce, industry, and also, it may be hoped, to the investigators themselves. To the successful essayist who, in the opinion of the Council of the Society of Chemical Industry, has shown conspicuous merit there will further be awarded a research fellowship of £300 per annum tenable at the discretion of the Council for two or three years. This fellowship, the gift of Sir T. P. Latham, Bart., is particularly intended to promote the study of economic botany, especially in its bearings on chemical industry; but the founder has with great wisdom and foresight allowed great latitude as to the nature of the researches on which the recipient of the scholarship may engage. This enlightened action ought to serve to stimulate some of the best among the younger men and to direct their attention to the rich fields of investigation that are awaiting them. Rubber, indigo, tea, oils, vegetable proteins, bamboo and forest refuse, especially abroad, and a host of other products at once suggest themselves as suitable subjects, and it must not be forgotten that investigations not only of the main substances, but of the by-products also, as all experience abundantly proves, are of immense value from a material and scientific point of view. The foregoing are, however, only a very few of those that might be quoted. The large and increasing lines of production that depend on vegetable organisms and fermentation only call for

a passing mention, inasmuch as they have recently been so ably dealt with in this JOURNAL by Mr. Chaston Chapman. The demand for vegetable oils and fats is a growing one, and the sources of supply are likewise increasing, while chemical investigation has already shown how much can be done in rendering the raw oil suitable for foods and other purposes. But we are really only on the threshold of the wealth which the vegetable kingdom holds out to those who know how to grasp it. As in utilizing these things we are increasing the revenue, without, as in some of our large industries, depleting the capital of the world.

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### CAMPBOR PRODUCTION IN BRITISH EMPIRE.\*

(Alfred Nutting, clerk in American Consulate General, London, England, April 11, 1920.)

The world's annual requirements and the present practical monopoly of production by Japan of camphor, together with the present high price and increasing demand, have drawn attention to the possibilities of profitable cultivation of camphor in other countries and particularly within the British Empire.

Prof. P. Carmody, F.I.C. (late Director of Agriculture, Trinidad), discusses the situation in the *Times Trade Supplement* of April 10. He points out that refined camphor is now about 2s. (\$0.49) per ounce and 23s. 6d. (\$5.72) per pound, whereas five years ago it was per pound little over the current price per ounce; and although there are, or have been, great fluctuations, the price may rise further unless increased production is assured.

Commercial camphor, he states, chiefly originates in Formosa, but as "the camphor is obtained there by distillation of the wood the annual destruction of trees must be very considerable, and this may account for the reports of diminishing supplies." It is estimated that 10,000,000 pounds of camphor are required by the world annually. Other present sources are the Fukien Province of China, Shikoku and Kiushiu Islands in Japan, Cochin China, Sumatra, Java and Borneo.

Results Already Obtained in British Colonies.—In 1852 the tree was introduced into Ceylon, but little more was done until in 1893 a supply of seeds was obtained from Japan, and 1,000 trees

\* From *Commerce Reports*, MAY 4, 1920.

were grown therefrom, from which, in 1901, the yield of solid camphor from fresh prunings was about  $1\frac{1}{2}$  per cent. "It is estimated," Prof. Carmody states, "that the yield of prunings (6 to 8 inches long), would amount to 56,000 pounds per acre per annum, and that with camphor at 2s. per pound the net profit per acre per annum would amount to £74 (\$360.00)." In 1906 there were over 100 acres devoted to camphor growing in Ceylon, but the cultivation was not commercially successful, as less than 1 ton of crude camphor was harvested.

At the present time experiments, with satisfactory distillation tests, are being carried out in the Federated Malay States, but in Mauritius the oil yielded is not the camphor of commerce.

In 1906, Prof. Carmody states, some 50 trees in Trinidad were transplanted to a better soil, with the result that "The growth has been quite satisfactory and a normal yield of solid camphor has been obtained on distillation," and in Dominica trees "obtained from Trinidad in 1911 have made satisfactory growth and have yielded solid camphor."

Requirements of Successful Cultivation.—In the matter of successful cultivation, he advises that "seeds or seedlings from trees that yield no solid camphor must not be used. Stiff clay soils must be avoided. Not more than 300 trees to the acre should be grown in good average soil, or not less than 12 feet apart in hedgerows, and a sufficient area (from 100 to 500 acres if possible) for economical distillation. When the trees are 4 or 5 years old they can be clipped, and thereafter three or four times a year."

Finally, he expresses the opinion that "the successful cultivation of camphor within the Empire is no longer doubtful," and "the reported depletion of native forests offers great inducements for further efforts," particularly in view of present high prices.

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## NOTE ON OPIUM POISONING.\*

BY H. E. HANKIN, M.A., D.Sc., AND D. CHATTERJI.

During the last three years stomachs, with their contents, of fifty-three persons have been examined in this laboratory, in which the history of symptoms and other evidence obtained by the police indicated that opium was the cause of death.

\*From *The Analyst*, May, 1920.

The results of analysis were as follows: In one case no opium was detected, but opium was found in the viscera of another person who had been poisoned at the same time; in four cases the results of analysis were consistent with the presence of traces of opium; in twenty cases traces only of opium were detected; in nine cases opium was detected in small quantity; in ten cases opium was detected in medium quantity; in nine cases opium was detected in quantity.

By the term "small quantity" we mean that the residue obtained from a Stas-Otto extract gave color reactions about as strongly as would the Stas-Otto extract of 7 Mgm. of Indian opium of 2 per cent. morphine content. The term "medium quantity" similarly corresponds to about 15 Mgm., and "detected in quantity" corresponds to 20 or more Mgm.

Thus there was a clearly negative result in one case. Out of the remaining fifty-two cases, in twenty-four opium was either detected in traces or the tests were responded to so faintly that no definite statement could be made as to the absence or presence of the poison. That in such a large proportion of the case opium should only be detected in traces appears to be in accord with results obtained by other observers (see Witthaus, "Manual of Toxicology," second edition, p. 980).

The only tests we have found to be of use in testing for opium in viscera are the following:

(1) *The Porphyroxin Test.*—We have carried out this test on several thousand extracts of viscera and other substances without ever getting a well-marked reaction, except in cases in which it was probable, on other grounds, that opium was present. On the other hand, a faint pinkish color occurs not infrequently in the absence of opium.

(2) *The Husemann Reaction.*

(3) *The Urotropin or Formaldehyde Reaction.*

This last-mentioned test has been used as a colormetric test for morphine in viscera (*Analyst*, 42: 227, 1917). But, in our experience, there are grounds for doubting whether either this test or any other known to us can be depended on to give reliable colormetric result. The viscera are always sent to us preserved in alcohol. In the hot Indian climate it often happens that much decomposition has set in before the viscera are placed in alcohol. With such viscera we find that if an extract responds strongly to one of the above three

tests there is no certainty that it will respond strongly to the others. The extent of this discrepancy is shown by the following table. It refers to analyses of thirty-one stomachs, three specimens of vomit, one of liver, and one of urine, a total of thirty-six specimens. In each case the history of symptoms, etc., had pointed to opium poisoning:

Reaction given by the Urotropin Test.		Reactions given in the same case by	
		Porphyroxin Test.	Husemann Test.
Strong in 8 cases.....	Strong	2	7
	Medium	5	0
	Negative or Doubtful	1	1
Medium in 16 cases.....	Strong	4	3
	Medium	12	13
	Negative or Doubtful	0	0
Doubtful in 6 cases.....	Strong	0	1
	Medium	5	4
	Negative or Doubtful	1	1
Negative in 6 cases.....	Strong	0	0
	Medium	6	6
	Negative or doubtful	0	0

Thus, in eight cases in which the urotropin reaction was strong, the porphyroxin reaction was only given strongly in two. In six cases the urotropin test gave a negative result, and in each of these the extract reacted with medium strength to the porphyrodin and Husemann tests. There can be little doubt that the cause of the occasional failure of the urotropin test is the inevitable presence of impurities in the extracts. It appears to be particularly difficult to get a pure extract in cases of opium poisoning. If an extract has a yellowish color there is a presumption, in our experience, that it is going to respond strongly to the tests for opium,

When dealing with highly decomposed viscera preserved for a fortnight or more in alcohol, no amount of washing with ether or with ether and chloroform will so purify the acid solution that it will not allow impurities to pass into the solvent when made alkaline. Repeated washing of the acid solution with ether is likely to result in the porphyroxin test yielding a negative result, and a valuable piece of evidence will thus be lost. Hence, in carrying out the Stas-Otto process, we wash the acid solution once only with ether and chloroform. It is advisable to add these solvents separately.

One part of chloroform is first added, then about three parts of ether, then a piece of litmus paper, and lastly, a few drops of ammonia. The mixture is then immediately shaken. We find that chloroform and ether thus used yield a purer extract than either an ethyl acetate-ether mixture or amyl alcohol.

GOVERNMENT LABORATORY, AGRA, INDIA.

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### JAMES E. BARTLETT.

The subject of this sketch, James E. Bartlett, has recently been elected President of Parke, Davis & Co., to succeed the late Frank G. Ryan. The elevation of any man to such a commanding position as the executive head of the leading pharmaceutical manufacturing corporation in the United States with its numerous branches scattered throughout the world, is worthy of more than a mere passing comment, as it is no slight compliment to the individual and is indicative of his personal qualifications and exceptional ability.

James E. Bartlett commenced his business career, while only a lad, as a clerk with Marshall Field & Co., of Chicago. After spending a year or two in this establishment at a nominal salary, with scant prospects for material advancement, he decided to leave Chicago and seek success elsewhere. He came to Detroit in 1889 and sought employment with Parke, Davis & Company. Although then but a mere youth, he was detailed as a salesman on the road, at which he made good. After spending a year or so in selling pharmaceuticals, he recognized, of his own accord, the need for a better acquaintance with the art of pharmacy and the advantages that might accrue to him from a more intimate knowledge of materia medica, even though he continued to apply his special efforts to the commercial side of the drug business. With this thought in mind, he temporarily left Parke, Davis & Co. and came to Philadelphia to attend the Philadelphia College of Pharmacy. On returning to Detroit he resumed his employment with that firm and spent several months in the various laboratory departments and was thus enabled to dovetail the knowledge acquired at the College with practical manufacturing experience.

His fidelity and ability won continual advancements and his promotions quickly followed each other and he had an unusual wide





*J. C. Brattle*



range of experiences in these various assignments. After serving as Assistant Foreman of the Pill Department, he was made Buyer, then Chief of the Fire Department, then Assistant Superintendent, and later Superintendent of the Laboratory; the latter important position he filled for a number of years.

In order to serve their customers more promptly and to increase their business in the Middle West, the house determined in 1896 to establish a branch house in Chicago. Mr. Bartlett was selected as the manger of this office and in a very few years the Chicago branch, under the impulse of his management, became an important center of the business.

In 1913, Mr. Bartlett was brought back to the Detroit headquarters to assume an executive position in the management. He was placed in charge of the selling division of the business and the whole organization soon felt the force of his dynamic personality. New sales methods were inaugurated; new products were pushed to the front; and the hum became more energetic and in harmony with the enthusiasm of the man at the helm.

A strong, self-reliant man, full of initiative and enthusiastically aggressive, Mr. Bartlett has always shown a natural capacity for leadership such as few men possess. His election to the presidency of the corporation brings him to the top after a steady climb up the ladder during a period of thirty-one years. Having grown up in the establishment, being personally acquainted with the details of the various departments and the personnel of the large body of employees, he is well equipped for the arduous duties now imposed. He is essentially a Parke, Davis & Co. product and typical of the business that he has so faithfully served.

In recent years Mr. Bartlett has taken an active interest in the American Drug Manufacturers' Association and at the meetings of that forceful organization he is a commanding figure. As chairman of the Committee on Commercial Travelers he presented a very interesting report. He is a member of the Executive Committee and has been a factor in shaping the policies of the Association in recent years.

He has been a regular attendant at the meetings of the National Wholesale Druggists' Association, and is well known to the wholesale and jobbing drug trade.

Since he became president of Parke, Davis & Company, he has initiated a number of forward-looking policies and has already made

his impress upon the organization. He has established an attendance bonus for the rank and file of employees and increased the annual vacation allowance; in addition he has provided that the older employees receive a cash vacation allowance annually. By one means or another he has impressed his personality and succeeded in increasing the enthusiasm and loyal support of the house by everybody concerned therewith.

In a recent editorial contributed to the *Oil, Paint and Drug Reporter*, Mr. Bartlett demonstrates that he is an optimist and has no sympathy with the calamity howlers. He holds that there is no cause for the alarmist or for a pessimistic view of the industrial and financial condition in the United States. In his opinion "There is not, at the present time, a serious cloud on the horizon, so far as the permanent future prosperity of the drug industry is concerned."

He has the real spirit and is representative of the type of men that must be the leaders in American commerce.

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## CURRENT LITERATURE.

### SCIENTIFIC AND TECHNICAL ABSTRACTS.

**OIL OF RUBIEVA MULTIFIDA.**—A specimen of the essential oil of *Rubieva Multifida*, distilled experimentally by the W. J. Bush Citrus Products Company, at National City, California, from the wild plants growing in the state, was examined.

The oil is light yellow in color and has an odor suggesting anise and terpenes.  $d_{25}^{25} = 0.8542$ .  $[\alpha]_D = +35.75^\circ$  (100 mm. tube).

On the first distillation about 60 per cent. comes over at  $37-40^\circ$  (under 3 mm. pressure). On repeated refractionation, about 85 per cent. of the oil was found to consist of a terpene fraction which, after rectifying over sodium, boils at  $169-171^\circ$  (under atmospheric pressure).  $d_{20}^{20} = 0.8507$ ,  $[\alpha]_D = +46.4^\circ$  (100 mm. tube).

The terpene fraction polymerizes rapidly on boiling at atmospheric pressure, has an odor resembling that of phellandrene, and yields a nitrosite melting at  $103-104^\circ$ . Hence it consists largely of  $\beta$ -phellandrene,

From the higher boiling portion of the oil anethole was separated. A resinous residue, probably polymerized phellandrene, was left on distillation. E. K. Nelson, Essential Oils Laboratory, Drug

Division, U. S. Bureau of Chemistry, Washington, D. C. (through *J. Amer. Chem. Soc.*, June, 1920).

**DETECTION OF MINUTE QUANTITIES OF PETROLEUM SPIRIT IN VEGETABLE OILS.**—A number of methods for the detection of petroleum spirit in vegetable oils have been proposed. A careful study of these has shown that they are not satisfactory, but it has been found that Nastjukoff's formolite reaction may be applied successfully for the purpose as follows:

The oil (50–100 g.) is saponified by means of potassium hydroxide solution. Distilled water and pure calcium chloride solution are added, the liquid distilled by means of steam, and the distillate treated with 40 per cent. formaldehyde solution and a few drops of concentrated sulphuric acid. A reddish brown film coloration on the surface of the liquid, gradually changing to deep yellow, indicates presence of petroleum spirit. If a few drops of the distillate are added to water, a brilliant interference ring of optical waves is produced on the surface of the water; this ring becomes almost invisible after standing for some time and disappears completely on heating. With soya bean oil the ring does not change, even on heating. The above process is capable of detecting traces of petroleum spirit in vegetable oils, and may be made the basis of a quantitative method, the formolite precipitate being weighed after drying at 110–115° C. Masahiro Aida. (From *J. Soc. Chem. Industry*, June 15, 1920.)

**CYSTINE REACTION.**—Cystine, whether present as a cystine calculus or in any other form, can be rapidly and easily identified by the following simple test: Place a small portion (not more than a milligram) on a slide, moisten with a droplet of strong hydrochloric acid (s. g. 1.17 to 1.18), and examine under the microscope without covering with a cover-glass; an abundance of groups of prismatic needles appear. Add a droplet of water; the slide clears. Evaporate at a gentle heat to dryness, cool thoroughly, cover, and add a droplet of water; after a few moments hexagonal plates appear.—Denigés (*Bull. Soc. Pharm. Bordeaux*, 58, 8; through *Pharm. Jour. and Pharmacist*, July 3, 1920).

**COLORLESS VARIETY OF MERCURIC IODIDE.**—Mercuric iodide may be obtained, temporarily, in colorless crystals, as follows: About 10 Gms. of the salt is placed in a long tube, sealed at one end,

and connected with a large vessel at the other, and heated to 300–350° C. The pressure is suddenly reduced to about 7 mm., when the mercuric iodide sublimes into the large vessel and condenses as a white snow, which in a few seconds becomes rose-pink, and ultimately the usual bright red color. By cooling the large vessel previous to the experiment the sublimate may be caused to preserve its colorless form a longer period. The yellow variety of mercuric iodide becomes colorless at the temperature of liquid air.—G. Tamman (*Zeitschr. anorg. Chem.*, 1920, 109, 213; *J. Chem. Soc.*, 1920, 118 (11), 315; through *Pharm. Jour. and Pharmacist*, July 3, 1920.)

FERRIC CHLORIDE TEST FOR DIACETIC ACID.—When testing the urine of a patient who had been taking sodium bicarbonate for gastric hyperacidity, Maxwell noticed a red color with ferric chloride similar to that obtained with diacetic acid. As there was no reason in this particular case to suspect acidosis and as the reaction of the urine was intensely alkaline, it occurred to Maxwell that the sodium bicarbonate might be the cause of the red color with ferric chloride. Repeated tests showed that if sodium bicarbonate were added to normal urine and then ferric chloride, the urine became a similar red color to that obtained in the presence of diacetic acid. In further experiments the urine of the author after ingestion of approximately 6 Gms. of sodium bicarbonate during a period of twenty-four hours, also gave a red color on the addition of ferric chloride. Presumably the ferric chloride reacts with the bicarbonate to form ferric hydroxide, which dissolves in the excess of ferric chloride to give the red color, carbon dioxide being evolved during the reaction. The more bicarbonate present, the deeper the red color produced. In all cases of acidosis which are being treated with alkalis, it is essential to exclude the possibility of sodium bicarbonate being responsible for the development of the red color when ferric chloride is added to the urine. If this precaution be overlooked, the dosage of alkali may be increased in the hope of overcoming an acidosis which in reality does not exist. (*Med. Jour. of Australia, Sydney*, May 15, 1920; through *Jour. Amer. Med. Assoc.*, July 17, 1920.)

DETECTION OF METHYL ALCOHOL IN SPIRITS: P. Hasse.—The sample is distilled and 0.5 Cc. of the distillate (containing not more

than 0.025 Cc. of alcohol) is mixed with 1 Cc. of 5 per cent. potassium permanganate solution, 2.5 Cc. of dilute sulphuric acid (sulphuric acid, 19 Gms., water 200 Cc.), and, after standing two minutes, the mixture is decolorized by the addition of 1 Cc. of 10 per cent. oxalic acid solution. To 0.5 Cc. of this mixture are then added 1 drop of peptone solution (= 2.5 Mgm. of peptone), and 1 Cc. of sulphuric acid containing iron (0.05 Gm. of iron alum dissolved in 1 Cc. of water and added to 300 Gms. of sulphuric acid). A deep blue color is obtained if the spirit contained 1 per cent. of methyl alcohol; a red-blue color is produced by 0.3 per cent. of the alcohol. Pure ethyl alcohol gives a yellowish red coloration with the test. If an indication of the presence of methyl alcohol is obtained, it should be confirmed by the morphine and magenta-sulphurous acid tests. (*Pharm. Zentr.*, 61: 177-182, 1920; through *J. Soc. Chem. Ind.*, 39: 345A, 1920; through *The Analyst*, June, 1920.)

(DETECTION OF CINNAMIC ACID.—Traces of cinnamic acid, either free or as a salt or ester, can be detected by means of a ferric salt and hydrogen peroxide. To every 2 Cc. of a solution of cinnamic acid or a cinnamate one drop of solution of ferric chloride is added and the mixture heated to boiling; one drop of hydrogen peroxide is then added and the tube shaken for a few seconds; if no odor of benzaldehyde is developed the tube is again heated to boiling. It is possible by this means to detect 0.02 Gm. of cinnamic acid in a liter of water; if the amount present exceeds 0.1 liter the quantity of ferric chloride and hydrogen peroxide may be doubled. Cinnamic esters should be boiled with 5 Cc. of water and two or three drops of solution of soda for twenty to thirty seconds and acidified with diluted sulphuric acid; the ferric chloride is then added, the mixture boiled, the hydrogen peroxide added, and again boiled, when the odor of benzaldehyde will easily be detected. A similar procedure is adopted with balsam of Peru or tolu. (M. G. Denigès, *Bull. Soc. Ph. Bordeaux*, 57: 209; through *The Pharm. Jour. and Pharm.*, Feb. 14, 1920.

SERUM TEST FOR ECHINOCOCCUS DISEASE.—Gasbarrini applied the test by the intradermal technic and obtained a positive response in all his twelve cases of hydatid cyst, except in one case in which the cyst had supplicated and thus had ceased to be "active." He commends the ease and harmlessness of the test. It is made with serum from bovine hydatid cysts, filtered; after addition of one

drop of phenol to 20 Cc. of the fluid it is set on ice. It keeps active for about a month. Giani obtained satisfactory results also with the Abderhalden test applied to human and bovine serum from subjects with echinococcus disease, and it was positive in seven of Gasbarrini's twelve cases. After surgical intervention the intradermal reaction veers to negative. (*Jour. Amer. Med. Assoc.*, Feb. 21, 1920.)

CULTURE MEDIUM SUITABLE FOR GROWTH OF ORGANISMS USED IN VACCINES.—Various types of culture mediums were prepared and examined by Norris with a view to the determination of their nutritive value as regards the growth of *B. typhosus* for vaccine purposes. Of the various meat mediums at present in use, those prepared by means of a tryptic digestion appear to be much more nutritive than an ordinary beef peptone medium or than those prepared by acid hydrolysis. The addition of nutrose and casein appears to have no great influence on growth unless added to a particular non-nutritive medium. The addition of a comparatively small amount of hydrolyzed nutrose to a poor medium increases the growing power to the level of an ordinary trypsinized medium. Glucose seemed to inhibit growth. Mediums obtained by the tryptic hydrolysis of nutrose, press cake from ground nut, and casein give material equal in nutritive value to that obtained from meat. In examining the nutritive value of these mediums, concentration of substrate appeared, within limits, to be of greater importance than time of hydrolysis. (From *Indian Jour. of Medical Research*, Calcutta, Oct., 1918, through *Jour. Amer. Med. Assoc.*, Feb. 28, 1920.)

POISONOUS ACTION OF BORAX ON PLANTS.—*Circular 84* of the United States Department of Agriculture gives an account of the extensive injury done by fertilizers containing notable amounts of borates. The cessation of imports of German potash brought about active search in the United States for sources of the material and several such were found, among them the deposits in Searles Lake, California. This contains notable amounts of borates, equivalent in some samples to 6.25 per cent. anhydrous borax in the potash as marketed. Large quantities of this potash were used in making complete fertilizers and applied to fields in which especially potatoes and cotton were grown. Great damage resulted, and the



investigations of the Department of Agriculture have shown that the borates were to blame. The salt was found to be particularly inimical to germination. The manufacturers of the Searles Lake potash have recognized the danger and are now marketing a product containing very little borate. It is evident that any new source of potash will have to be carefully examined for this objectionable compound.

H. L.

RAPID METHOD OF ESTIMATING LEAD IN CASSIA OIL.—O. F. Lubatti. (*J. Soc. Chem. Ind.*, 39: 35-36T, 1920.)—Cassia oil exported from China is contaminated with lead derived from the leaden vessels in which it is sold. For the rapid colormetric estimation of this lead by means of ammonium sulphide 5 Cc. of the oil (or 2.5 Cc. if a preliminary test has indicated the presence of more than 0.025 per cent. of lead) are diluted to about 23 Cc. with 90 per cent. alcohol in a Nessler cylinder of narrow diameter (2.5 Cm.). The same amount of cassia oil free from lead is diluted in the same way in a second tube, 1 Cc. of ammonium sulphide solution added to each liquid, and a standard solution of lead in 90 per cent. alcohol (1 Cc. = 0.0001 Gm. Pb) is added to the blank until it matches the brown coloration of the sample under examination. The liquid is stirred three times after each addition of lead solution. The results thus obtained are slightly high, the average excess being 0.00018 Gm. The amount of lead usually present in commercial samples ranges from 0.04 to 0.06 per cent. In a test experiment, in which a pure oil was left in contact with bright lead in closed tubes, which were shaken at intervals, the maximum absorption of lead was 0.074 per cent., and was reached after one month. (From *The Analyst*, April, 1920.)

TESTING THE AMYLOLYTIC ACTION OF THE DIASTASE OF *Aspergillus Oryzae* (TAKA-DIASTASE).—S. A. Waksman (*J. Amer. Chem. Soc.*, 42: 293-299, 1920).—The various diastatic enzymes differ in their mode of action towards starch, particularly as regards the relative quantities and rates of formation of the intermediate and final products. In this sense it is convenient to differentiate between the amylolytic (liquefying) and the saccharifying powers of the commercial diastatic preparations. The measurement of saccharifying power has formed the subject of many exact researches but the measurement of amylolytic power leaves much to be desired in the

way of refinement, and this property is the essential one in the valuation of diastatic enzymes applied to the textile industry. The Lintner method for measuring the saccharogenic action should not be used for comparative studies of different enzymes, since the end products are not the same in all cases. Most of the methods hitherto employed for estimating the starch liquefying power depend on the use of iodine for determining the end-point, and the indications are somewhat arbitrary. In the method now described the end-point taken to indicate the complete destruction of the starch is the change of the opaque starch paste into a clear solution. To facilitate the recognition of this point it is found to be convenient to dye the starch with neutral red. About 50 to 100 Gms. of dry potato starch in a large porcelain dish are wetted with 100 Cc. of a 0.5 per cent. solution of neutral red; the starch is allowed to absorb all the color, and then washed repeatedly with water until the supernatant liquor remains almost clear. The dyed starch is then dried. For the test a 2 per cent. starch paste is made by stirring the colored starch with a little cold water, gelatinizing with boiling water, boiling for ten minutes, and making up to the required volume. The paste is introduced in portions of 10 Cc. each into large test-tubes, which are then placed in a thermostat at 40° C. When the correct temperature is reached, increasing quantities of the diastase solution are added to the tubes, and these are well shaken and replaced in the thermostat. The end of the reaction, indicated by the clearing up of the color, is best observed by comparing the liquefied and unliquefied tubes, holding the tubes in the light. The times (T) at which the various tubes become clear are recorded in conjunction with the quantities of enzyme solution (E) present, and it is found that  $E \times T = a \text{ constant } K$ . Then if F = enzyme value at 40° C.; D = dilution multiple of the original enzyme solution; t = standard time (30 minutes); E = quantity of diluted enzyme solution used; and T = the corresponding time of liquefaction

$$F \frac{30 \text{ min.}}{40^\circ} = \frac{D.t}{E.T.} \text{ or } \frac{D.t}{K}.$$

In this way the results may be checked by taking the average of several tubes containing different amounts of enzyme. The method is particularly suitable for the study of enzymes which have a starch liquefying power rather large in comparison with the saccharifying power, as, for instance, "Take-diastase." (From *The Analyst*, April, 1920.)

DETECTION OF INDICAN IN URINE AND BLOOD.—A. Jolles (*Med. Klinik*, 15; 814, 1919; through *Chem. Zeit. Übersicht*, 44: 37, 1920).—Instead of converting the indican into indigo according to the methods of Obermayer and Jaffé, the author recommends the following method: The indican of urine consists principally of potassium indoxylsulphate, which when submitted together with thymol to oxidation by means of ferric chloride yields 4-cymol-2 indolindolignon. This substance forms with one molecule of hydrochloric acid a deep violet dye, which is produced when the chloroform extract of the urine or blood is treated with thymol, fuming hydrochloric acid and ferric chloride. (From *The Analyst*, April, 1920.)

MICRO-METHOD FOR THE ESTIMATION OF ACETONE.—M. Richter-Quittner (*Biochem. Zeitsch.*, 93: 163-172, 1919; through *J. Soc. Chem. Ind.*, 39: 206A, 1920).—A micro-method in which 1 to 2 Cc. of urine and 1.5 to 3 Cc. of alkali need only be used. The urine is distilled once with steam in the presence of acetic acid and a second time with dilute sulphuric acid. Blood or plasma need only be distilled once, and instead of the steam, air is passed through the heated flask. The titration of the distilled acetone is carried out with *N*/10 iodine and *N*/100 sodium thiosulphate; 0.1 Mgm. of acetone in 100 Cc. can be estimated with accuracy by this method. The quantity of urine and blood used must not contain less than 0.04 Mgm. of acetone. (From *The Analyst*, April, 1920.)

CARAMEL.—G. P. Plaisance and Helen Monsch, of the Iowa State College and Agricultural Experiment Station, have studied the occurrence of furfural in caramel (*Jour. of Home Economics*, 1917, ix, 167-171). Caramel is used as a coloring, *e. g.*, in artificial vanilla extract, and is formed from sugar in cooking. Furfural, furfurole or furfuraldehyde is an heterocyclic aldehyde which is volatile in steam. It is somewhat toxic, thus 0.1 Gm. causes headache in man and 0.5 Gm. kills a cat or a rabbit. Some furfural is formed when sugars, especially cane sugar, are caramelized at a temperature ranging from 180° to 200° C.; the greatest production of furfural noted was 0.944 Gm. from 1 kilogram of cane sugar on carmelization for four minutes at 200° C. However, the furfural is completely expelled if the caramel be boiled with an equal amount of water for ten minutes in an open pan. No precautions to prevent the injurious action of furfural are necessary when the food is cooked in the presence of

water after caramelization, as in the preparation of cakes, frostings, and rice pudding. In candy-making the cooking should be conducted at as low a temperature as possible, since the yield of furfural increases with the temperature. Care should be taken to prevent caramelization in the baking of fruits; it is desirable to boil caramelized fruit syrups with an equal volume of water for ten or fifteen minutes before serving them.—(From *Jour. Franklin Institute* May, 1920.)

PROSOL, A NEW KETONE.—While engaged in an exhaustive examination of the grain of the proso (Russian) millet, with a view to determine its adaptability as a breadstuff and its possibilities as a food crop for the South Dakota west-of-the-river country, Professors B. A. Dunbar and E. R. Binnewies, of the chemistry department of State college, discovered an alcohol-ketone by-product which so far as they have been able to ascertain, has not been discussed in the literature pertaining to plant products. The product, pending its further examination, has been named "prosol."

The new alcohol is a most peculiar one, being one of those which are insoluble in water. The tentative molecular formula  $C_{24}H_{36}O_2$  has been assigned to the product.

The grain upon which the study was based was raised upon the State college farms from specially selected white seed derived by selection from mother seed obtained in Russia by Dr. N. E. Hansen. (*Journal of the American Chemical Society*, March.)

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#### NEWS ITEMS AND PERSONAL NOTES.

THE NATIONAL RESEARCH COUNCIL.—The National Research Council has elected the following officers for the year commencing July 1: Chairman, H. A. Bumstead, professor of physics and director of the Sloans Physical Laboratory, Yale University; First Vice-Chairman, C. D. Walcott, president of the National Academy of Sciences and secretary of the Smithsonian Institution; Second Vice-Chairman, Gano Dunn, president of the J. G. White Engineering Corporation, New York; Third Vice-Chairman, R. A. Millikan, professor of physics, University of Chicago; Permanent Secretary, Vernon Kellogg, professor of biology, Stanford University; Treasurer, F. L. Ransome, treasurer of the National Academy of Sciences.

The Council has recently received an endowment of \$5,000,000 from the Carnegie Corporation, part of which will be spent in the erection of a suitable building in Washington for the joint use of the Council and the National Academy of Sciences. Other gifts have been received for the carrying out of specific researches.

It is now beginning to function and has issued as Bulletin No. 2 a list of the research laboratories in industrial establishments of the United States. This bulletin gives a brief account of the organization and personnel of more than three hundred of such laboratories now maintained by our industries. It is interesting to us to note that many of the pharmaceutical manufacturers are listed in this catalogue.

The Council has likewise assisted in the organization of the Plant Protective Institute. The purpose of the Institute is to promote general welfare by supporting and directing scientific research on the pests of crops, shade trees, and ornamental plants, and on the methods of their control, and by furthering coöperation between the scientific investigators and the manufacturers of chemicals and appliances so as to effect standardization and economy.

CATALOGUE OF THE MONSANTO CHEMICAL WORKS.—The Monsanto Chemical Works, of Saint Louis, have issued a unique catalogue of their products. It is elegantly printed on tinted high-grade book paper with cover embossed in bronze and is an excellent piece of work from the view-point of the printers art. It is well illustrated with views of their several chemical plants and offices and from the front page beams in half tone the genial countenance of Mr. John F. Queeny, the founder and at present chairman of the board of directors to whose untiring energy and enterprise the success of this company is ascribed.

This catalogue is unique in that it contains no prices whatever but shows a list of the products, each being presented in a monographic style in which is set forth the chemical composition, physical properties and the standards, or specifications for purity, adopted by these manufacturers for their individual products. It is useless to state that these indicate a very high standard. The list includes many chemicals of medicinal use and pharmaceutical interest and of a great variety and types of manufacture. Among the coal-tar derivatives we may mention acetanilid, acetphenetidin, acetylsalicylic acid, phenol, phenolphthalein, salicylic acid, saccharin,

salol and the newer chlorine derivatives used as antiseptic wound dressings and as germicides.

They are also large producers of the mineral acids, chrome alum, and are well known in the trade for their development of the manufacture of glycerophosphates and the excellence of their productions of these medicinal chemicals. They also manufacture caffeine, coumarin, and are constructing a plant for the manufacture of synthetic camphor in large quantities. It is now well known that for the manufacture of celluloid and many similar products of industrial importance the artificial camphor serves as well as the natural. This will release for use in pharmaceutical preparations an enormous amount of the natural camphor which has theretofore been consumed in these industries and should result in further declines in price.

The success that has attended the efforts of this company to produce in the United States medicinal and fine chemicals which, before this company was founded in 1901, had been largely imported from Europe, has been as noteworthy as deserved and we consider this as a tribute to the skill, energy and indomitable enterprises and foresight of its management.

**H. K. MULFORD CO.'S PICNIC TO EMPLOYEES.**—For a number of years the H. K. Mulford Company have been giving an annual picnic to their employees and their families. This year this event, which has been termed "Mulford Day," was observed on June 19th, last. Special trains carried the excursionsists to the extent of several thousand to Glenolden. The day was given over to athletic events, music and dancing. Many of the visitors took advantage of the opportunity of inspecting the fine collection of horses in the stables, the biological laboratory and the drug gardens at Ridgway. Ample refreshments were served and the participants thoroughly enjoyed the occasion.

**LEHN & FINK, INC., IN NEW BUILDING.**—Lehn & Fink, Inc., who for many years conducted their business from their New York Office, 120 William Street, have now moved up town into their newly constructed modern steel and stone building at Greenwich, Morton and Barrow Sts. This is a seven-story fire-proof structure, and will, the firm thinks, provide the room which they need for the enormous development of their wholesale drug, manufacturing, and importing business.

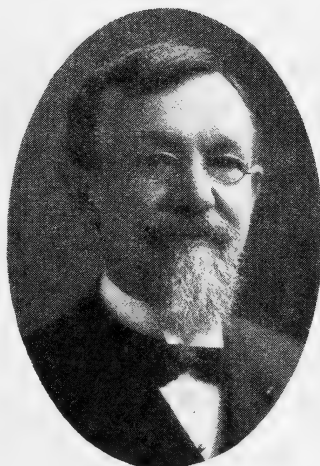
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## OBITUARY.

### EDWIN McCURDY BORING.

Edwin M. Boring, who died at his home in Philadelphia, June 22, 1920, was the son of John Dobbins Boring and Catherine McCurdy Boring, and was born at Lancaster, Penna., October 24, 1839. His boyhood days were spent in his home town, where he attended High School. Thereafter, about 1857, he worked for a time in Welchen's Drug Store, in Lancaster, and for a few months in Philadelphia, after which he returned to Lancaster.

He responded to Lincoln's call for 75,000 volunteers, and entered the three months' service with the Lancaster Fencibles, April 18, 1861. At the expiration of the three months he re-enlisted in Company E, 79th Pennsylvania Volunteers, first as private, and was commissioned First - Lieutenant June 19, 1864. He took part in a number of the great battles of the war, at Murfreesboro, Chickamauga, etc.



EDWIN McCURDY BORING

He was mustered out July, 1865. As a member of the Executive Committee of the State of Pennsylvania Chickamauga-Chattanooga Battlefields Commission he assisted in the erection of the monument at Chickamauga Park to the 79th Pennsylvania Volunteers.

After the war, September 4, 1865, he came to Philadelphia, and entered the employ of Edward B. Garrigues, at 10th and Fairmount Ave. During the same year he matriculated at the Philadelphia College of Pharmacy and graduated in the class of 1867. During the summer of 1866 he studied botany under Dr. Horatio C. Wood, of the University of Pennsylvania, then located at 9th and Chestnut Sts. He was elected to the Board of Trustees of his Alma Mater in 1868, and continued a member until the time of his death. In 1868 he formed a partnership with Mr. Garrigues, which continued until the time of the latter's retirement in 1887, when Mr. Boring became the sole proprietor. He continued this business until last year, when he disposed of it to his successor.

The deceased became a member of the American Pharmaceutical Association in 1867, and attended many of the annual conventions especially those of earlier years. He was one of the organizers of the Philadelphia Wholesale Drug Company, a member of the Pennsylvania State Pharmaceutical Association, and the Philadelphia Association of Retail Druggists.

October 8, 1873, Mr. Boring married Elizabeth Garrigues Truman, who died February 18, 1907. They had four children, all of whom survive the deceased. They are Edwin Garrigues Boring, Professor of Experimental Psychology in Clark University, Worcester, Mass.; Alice Middleton Boring, for the past two years Assistant Professor of Biology at the Union Medical College, Peking, China, and now appointed Assistant Professor of Zoology at Wellesley College, Wellesley, Mass.; Katharine Boring Rondthaler, wife of Dr. Howard Rondthaler, President of Salem College, Winston-Salem, N. C.; and Lydia Truman Boring, Assistant in the Psychiatric Clinic of the Home Service Section, S. E. Penna. Chapter, American Red Cross.

The deceased was a member of the Moravian Church, and took an active part in its affairs. As a citizen he stood for what is best in civic life; in the family his example as husband and father made for what is best in the home circle; his loyalty, sense of duty and obligation to pharmacy marked his life with success.

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E. G. E.



# THE AMERICAN JOURNAL OF PHARMACY

SEP 20 1920  
SEPTEMBER, 1920

## EDITORIAL.

### IS THE PRACTICE OF PHARMACY TO BECOME A NEGLECTED ART?

Under the title "Why Proprietaries Flourish" the following letter is published in *The Journal of the American Medical Association* for June 2, page 558:

"To the Editor:—The following experiences seem to add one more to the many reasons offered to explain why proprietaries and ready-made preparations flourish at the expense of the official drugs and preparations: A few days ago I prescribed Troches of Ammonium Chloride, U. S. P., for a patient of exceptional perseverance. The next day he had not yet secured the troches and told me that he had submitted the prescription to seven pharmacies, including the largest and three of the best known and admittedly the best equipped in New York. All told him that these troches were "Not being made any more," and that they were, therefore, unable to supply him. He thereupon communicated with one of the largest wholesale manufacturing pharmaceutical houses in America and received precisely the same answer. I then took the matter up with a first class pharmacist whom I knew and induced him to prepare this difficult(!) troche, for which the U. S. Pharmacopoeia gives the following directions: 'Rub the powders together until they are thoroughly mixed; then form a mass with syrup of tolu and divide . . .'

"Seven pharmacists declined to fill a prescription for an official preparation because they could not buy the preparation from a wholesaler, and it required some persuasion to get the eighth to make the preparation. But even, worse, several of the pharmacists offered my patient some ready-made troche more or less closely resembling the official, or offered compressed tablets of ammonium chloride.

"That this is not an isolated example of what often poses as pharmacy is shown by the fact that I have found it extremely difficult to find a pharmacist who would extemporaneously coat pills with gelatin. Most want the physician to alter his prescription so that one of the ready-made gelatin coated pills can be dispensed, if a gelatin coating is necessary. Some gelatin, hot water, a large cork, and a few domestic sewing needles are all that is required for very satisfactory coating of pills with gelatin, yet few pharmacists seem willing to perform this simple procedure.

"Two other illustrations, not so recent, have come to me from a colleague. A few years ago he was unable to obtain an emulsion of cod liver oil without the hypophosphites because, as both pharmacists said, 'It does not come without hypophosphites.' On another occasion four of the best drug stores in Boston were asked for the Compound Laxative Pill, U. S. P., then official in the Pharmacopoeia. In every case he was told that he must have meant the compound cathartic pill, which in no way resembles the pill he sought.

"With this attitude on the part of the men supposed to be serving the public and the medical profession by the practice of pharmacy, is it any wonder that it is difficult to induce the medical profession to prescribe official preparations or combinations of official drugs in place of ready-made commercial substitutes largely drawn from among the proprietaries or specialties? Real pharmacy by real pharmacists is a necessity if we are to succeed in combating the proprietary evil.

"CARY EGGLESTON, M. D., New York."

By this communication, Dr. Eggleston has performed a service to pharmacy and to a somewhat lesser degree also to medicine. His criticism of the attitude of the pharmacist referred to in his letter, is fully justified by the experiences detailed. Our inclination is to more strongly condemn their failure to discharge their professional obligations as we consider their action as detrimental to pharmacy and deserving censure in a most positive manner and in no uncertain language.

It is evident that Dr. Eggleston is an exception among physicians as his communication demonstrates a knowledge of pharmacopoeial formulas which is certainly unusual among prescribers. After all, can we not trace these experiences to the initial fault, the fundamental error; the defect in the education of physicians by reason of which they become so little acquainted with the official *materia medica*.

and the formulas and dosage forms for the accepted medicines that many of them almost entirely neglect these for the proprietaries or the ready-made "specialties" of the manufacturing houses which frequently are but other forms for exhibiting the same medicines. If the physicians were properly educated and prescribed the official medicines to the fullest extent possible, doubtless a sufficient number of pharmacists would be equipped to promptly dispense every prescription calling for these.

It is a sad commentary upon the present status of the medical practices that we must admit that a number of the pharmacopoeial preparations, standard remedies, are so completely neglected and ignored by the medical practitioners that some of the druggists appear to have entirely forgotten that the titles and formulas for these are in the U. S. P. These formulas, no matter how desirable they may be from a therapeutic standpoint, are becoming obsolete from non-use and sooner or later must be deleted from the Pharmacopoeia and possibly even from the National Formulary. The existing condition unquestionably calls for corrective measures and these can be effected only by the earnest coöperation of the exponents of the professional practice of medicine and pharmacy.

In pointing out this fundamental error in the medical education of the time, we are fully aware of the fact that Dr. Eggleston in this communication points out, in a courteous yet forceful manner, vital defects in the education and practices of pharmacists. It is not our purpose to excuse these in the least, neither is it our intent to minimize the force of his criticism, but rather add thereto. It is deplorable that in this progressive and scientific age and after nearly a century of systematic efforts in behalf of pharmaceutical education, such episodes can be recorded. It is almost inconceivable that such incidents could occur in the large cities like New York and Boston and be reported as happening in the "largest," "best known" and "best equipped" pharmacies in the leading American metropolises. In an urban community or in a back-wood's district one might be more charitable in his criticism. From the view point that we entertain of the ideals of professional pharmacy, we must attribute the experiences described by Dr. Eggleston either to woeful ignorance, professional stupidity, business inaptitude or unsophisticated indolence and none of these are valid excuses or excusable.

The official troches of ammonium chloride require no special apparatus, unusual materials or exceptional skill for their prepara-

tion and even if a lozenge board or a lozenge cutter is not in the equipment, the troches can be readily made extemporaneously with the common utensils, mortar, pestle and spatula which are necessarily at hand in every drug store. The Pharmacopoeia, presumable for self-evident reasons, gives very simple instructions for the manipulation in this formula and leaves to the judgment and the art of the dispenser the method of dividing and even the shape of the troche so that he is at liberty to improvise in these matters as occasion may require. The preparation of emulsions of cod liver oil, compound laxative pills and of gelatin coated pills on prescription, requires no unusual skill or exhibition of the art of the apothecary and every graduate of a school of pharmacy should have been taught in the school not only the theories of such operations but acquired by practical work the skill essential to compounding such on physician's prescriptions. The processes named are merely practical exhibitions of the art of pharmacy and not beyond the ability of a tyro.

They are in the line of the professional duty of the pharmacist and the service which he owes to society and constitute his part in the great medical professions. When these so called pharmacists failed to perform their bounden duty and to practice the true art of pharmacy, they injured not themselves alone but the entire profession of pharmacy. Without the proper exercise of the art and the development that comes from actual practice there can be no progress of the profession. It is humiliating to those who have devoted their best efforts in behalf of pharmacy that such incidents should occur. The pharmacists of America and especially those associated with pharmaceutical education, should take from Dr. Eggleston's communication a timely lesson as to the insufficiency of, and defects in pharmacuetical education and practices.

G. M. B.

#### A QUESTIONABLE DECISION.

Under the caption "Copyright Trade Mark Declared the Sole Property of the Centaur Company," the *Canadian Druggist* for July, 1920, informs its readers that: "In the Practice Division of the Superior Court, Mr. Justice Duclos delivered judgment in the case of the Centaur Co. *vs.* the American Druggists' Syndicate, Ltd., enjoining the use of the name Castoria in connection with the sale of any medical laxative preparation not manufactured by the Centaur Co."

Upon the text of this decision as given in the editorial the following comments are made.

"The title of the editorial, and the comments of the editor, and also the decision of the Court are at variance with what seems to be the law relating to copyright, patents, and trade-marks, not only in the United States, but in Great Britain, and its Colonies. The editor seems to have a confused idea in regard to copyright, or the right to copy the published writings of writers and the unpatented discoveries of inventors—rights possessed by everybody—and the exclusive right naturally possessed by every manufacturer to so mark his brand of goods as to inform the public concerning their source of manufacture. The text of the 'judgment' indicates that Mr. Justice Duclos shares in this confusion of mind.

"As stated in the Report of the Commissioners Appointed to Revise the Statutes Relating to Patents, Trade and other Marks, and Trade and Commercial Names, under Act of Congress Approved June 4, 1898 (Senate Document No. 20), p. 91: "There is no such thing as an exclusive right to any particular branch of industry. Any article of manufacture, unless it be protected by a patent, may be made and sold by any person. The only restriction is that each party shall stand upon his own merits, and none shall be permitted, by the use of marks or symbols, to pretend that the goods offered by him are the products of another.'"

The necessities of spoken and written language, the necessities of science, of the arts and manufactures, and of commerce, require that each new invention shall be provided with a name of its own by which it may be recognized and dealt in, and that such name shall be free to the use of all who have the right to make and deal in the article. This self-evident fact was well expressed by the Court in *Leclanche Battery Co. vs. Western Elec. Co.*, 23 Fed. Rep., 227, as follows: "When an article is made that was theretofore unknown, it must be christened with a name by which it can be recognized and dealt in, and the name thus given it becomes public property, and all who deal in the article have a right to designate it by the name by which it is alone recognizable."

Mr. Justice Duclos says: "After a careful consideration of the evidence, authorities and arguments submitted to me I find:

"1. That the petitioners secured a valid and still existing trade-mark in Canada."

*Comments.*—Castoria is the name of the product sold by the

Centaur Company, just as it would be if they were selling salt or sugar under the names "salt" and "sugar," respectively. It is axiomatic that a name cannot at one and the same time perform the function of a brand mark, and the name of the article itself. During the life of a monopoly, no matter how created, whether by secret formula or patent, only one brand is possible, and, therefore, the name given to the product can only distinguish between the product itself and other products of unlike character. But when the monopoly ceases, either by the disclosure of the trade secret, or by the expiration of patent, it may become advisable to adopt a word or mark to distinguish between the original brand, and other brands of the same article on the market, because the name of the article itself cannot perform that function. The name "salt" cannot distinguish between the various brands of salt on the market, and the same is true in reference to the name "sugar." And now that the working formula for the production of castoria (which was of course published by the inventor in his application for United States patent) is common property, any person has a right to manufacture castoria and sell it as castoria.

Certain trade mark lawyers have claimed that the commercial introducer of a new product can, by registering the name given such product as a trade mark, secure exclusive ownership of such name. On this hangs the entire fabric of the so-called proprietary medicine system. But this is an absurdity: The logical outcome would be to force each manufacturer of an unpatented product to coin a new name for it until the common language would become so loaded up with synonyms as to make it impossible for anybody to remember them. It would, in fact, necessitate a library building as large as a city public library to accommodate the dictionaries required. This is illustrated by "hexamethylenamine" for which there are already more than fourteen synonyms including "aminoform," "urotropin," "cystamin," "cystogen," etc.

"2. That the respondents have, and are intending to infringe this trade-mark."

*Comments.*—If the American Druggists' Syndicate is using and intends to use the name "Castoria" in such manner as to deprive the Centaur Company of its rights, or to deceive the public, then this statement of Mr. Justice Duclos is in accord with the facts. On the other hand, if it is using the word "Castoria" as the name of a product which is common property, and which all have an equal

right to make and sell under the name "Castoria," then the American Druggists' Syndicate in going into competition with the Centaur Company is acting within its rights, unless they are deceiving the public by imitating the packages of the Centaur Company. The correctness of the above statement is recognized by *Standard Remedies*, for Dec., 1915 (*Standard Remedies* is published in the interest of the manufacturers and jobbers of proprietary medicines, cosmetics, etc.).

In referring to the dangers attending the Goldwater Ordinance, the editor warns manufacturers to be careful not to jeopardize their trade-mark rights, by complying with the requirements of the New York health board until they are compelled to do so, if they ever are, by the decision of the Courts of last resort.

In support of this warning the editor quotes the following paragraphs from Cyc. 38-740:

"The name of a secret or proprietary preparation is descriptive thereof, and hence is not a valid trade-mark. Anyone who discovers the secret and makes the goods according to the formula may use the name to describe the goods. A contrary view has been expressed, and such names declared to be valid trade-marks, but such cases must be deemed instances of the broader doctrine of unfair competition. Of course the name may not be used to pass off spurious concoctions as and for the genuine preparations."

To again quote from Cyc. 38-835:

"The name of a secret and proprietary preparation will be protected against unauthorized use or imitation as the name of some other different preparation of like kind sold in competition, but not made in accordance with the formula of the original and genuine article, even though the labels and wrappers are entirely different, because such a use is necessarily false and deceptive.

"But such names are generally descriptive and therefore may be used by anyone who discovers and knows the secret of the composition of the article and makes his own article according to the original formula. If such is the truth a subsequent user of the same must add some distinguishing statement showing that the article is his own production of the article known by that name and he must not imitate the dress or the makeup of the goods in addition to using the name, or do any affirmative act calculated to deceive the public and pass off the goods as and for the previously known goods."

"3. That the name 'Castoria' is a purely fancy name in no way descriptive of the article."

*Comments.*—A fanciful name is one that is used fancifully. Is the name "Castoria" being used fancifully by the Centaur Co., or is it being used descriptively? The word "Castoria" in itself, means nothing, and the same is true of the words "cat," "dog," "hat," "buggy," "piano," and "porcupine." In themselves these words may be with equal propriety called fancy names. But when they are applied to the various things which have become known by these names they become, by such use, descriptive nouns of the common language. In this way "Castoria" has become just as descriptive of the medicinal preparation known as Castoria as the name "salt" is descriptive of salt, and the name "sugar" is descriptive of sugar.

"4. That in Canada the word 'Castoria' has acquired a secondary meaning identifying the article sold under that name as the manufacture of the petitioners."

*Comments.*—Now, when it is considered that the function of a trade-mark is to distinguish between brands, and that the name of an article cannot at one and the same time perform the function of an appellative and a brand mark, it becomes at once apparent that the name "Castoria" is not being used by the Centaur Co., as a trade-mark, and, therefore, is not in fact a trade-mark. The only reason why the name "Castoria" exclusively distinguishes the manufacture of the Centaur Co. is because the Centaur Co. has monopolized the sale of the product known as Castoria. Until the monopoly ceases there is nothing to distinguish it from. But when someone else commenced to make Castoria then two brands of Castoria came into being, and it logically follows that both brands must be sold under the generic name, *i. e.*, "Castoria," otherwise, the manufacturer of second brand is deprived of his rights, for he has an equal right to manufacture and sell Castoria, and would be deprived of that right if he could not sell it as "Castoria." It is evident that the manufacturer of the second brand would be forced to educate the public to use another name for "Castoria," claiming the preparation under the new name to be the same as that being sold by the Centaur Co., under the old name, and would also be obliged to do so under the unfair handicap of charges of fraudulent imitation.

"5. That no one in Canada can sell or offer for sale a senna laxative under the name of Castoria, without misleading the public



into the belief that they are selling the petitioners' goods while passing off their own."

*Comments.*—All that is required is not to imitate the packages of the Centaur Co., but to offer the product as Castoria under the label and package of the American Druggists, Syndicate, just as would be done in offering fluidextract of senna, or syrup of squill by competitors in the manufacture and sale of these products.

"6. That the article which the respondents are putting on the market as 'Castoria,' while very similar, is not the same product as manufactured by the petitioners, and, therefore, cannot be truthfully called 'Castoria.' "

*Comments.*—As already stated, the working formula for the manufacture of "Castoria" was published by the inventor when he obtained his United States patent, and is obtainable from the Patent Office for a nominal sum. If a person skilled in the art of pharmacy cannot reproduce the identical article by using this formula then the original patent was obtained by fraud. In that case neither the inventor nor his agents can go into court with clean hands to defend a suit for infringement. It might be well for the American Druggists, Syndicate to investigate this phase of the subject.

#### FURTHER COMMENTS AND SUGGESTIONS.

Contrary to general belief names cannot be copyrighted. To correct this misapprehension the Librarian of Congress issued circular number 19, which reads as follows:

"The Copyright laws contain no provision under which protection can be obtained upon a mere name or title. Entry cannot therefore be made in the Copyright Office for coined names; names of articles of manufacture; names of games or puzzles; names of substances, names of products, or names of medicines."

Neither can a name be patented. Its registration in the Patent Office as a trade-mark does not confer any right to its exclusive use as the name for an article of commerce. Such registration serves to give notice that the name registered is claimed as a trade-mark. If it is afterward used as the name of the article itself it becomes a title and not a trade-mark.

The same trade-mark may be used by as many manufacturers of different brands of goods as there are classes, for example the word "star" or the picture of a star has been registered for not less than four hundred classes of goods. As the classification of goods in the

Patent Office is merely arbitrary it is quite important, therefore, that a manufacturer should, for his own protection, accompany the word mark or brand name with the name of the article, on labels and in advertisements, so distinguished between them as to make it clear which name is claimed as a trade-mark, and which is the name of the article itself.

It was stated in a decision of the board of Examiners-in-chief, and appellate tribunal of the Patent Office, in the case of Caffall, MS. Vol. 18, p. 322, that:

"It was never intended that any new composition of matter or mixture of simples should be the subject of monopoly. If rhubarb and senna, or calomel and jalap were for the first time put together, he who should do it, whether regular practitioner, or quack, would not be an inventor or discoverer under the law. If done by a doctor it would only be the exercise of ordinary professional skill; if by another, it would be but an ignorant jumble of things having supposed virtues and benefits to be obtained by the union of known drugs."

A scheme is on foot to obtain such objectionable monopolies, and their protection by the Courts, by creating a system of patenting names in each country, and then by means of international treaties to form a union for the commercial control of such names throughout the world. Some of the Latin countries have already adopted this scheme. Further information concerning it may be obtained by consulting the Report of the Commissioners Appointed to Revise the Statutes Relating to Patents and Trade-marks (Senate Document No. 20), referred to above. The following paragraphs are copied from a report of a draft presented by M. Ch. Jagerschmidt, a French delegate to the Conference which met at Paris, Nov. 4, 1880, for the purpose of taking preliminary steps leading to the adoption of the International Convention at Paris, 1883, having as its object "the protection of patents for inventions and other industrial property." The Convention was ratified at Paris, June 6, 1884, but was not adhered to by the United States until March 29, 1887, and proclaimed by the President, June 11, 1887. Still our Government sent a delegate to the first conference under it, held at Rome in 1886.

The following paragraphs are copied from Mr. Jagerschmidt's draft:

"Art. 6. Every production bearing unlawfully either the mark of a manufacturer or of a merchant located in one of the countries

of the Union, or an indication of origin in such country, shall be prohibited entry in all the other contracting States, excluded from transit and from storage, and may be subject to seizure followed, if necessary, by a suit in court."

"Art. 8. The ownership of a commercial name shall be guaranteed in all the States of the Union without distinction of nationality and without obligation of deposit, whether or not it forms part of a mark of manufacture or of commerce."

"Articles claimed to be infringements may be seized in the inclosure of the expositions."

"The expense to which this institution shall give rise shall be borne by all the Governments of the contracting States."

The attempts to create a system of perpetual monopoly of inventions and alleged inventions by commercial control of their currently used names, and the establishing of an international method for obtaining proprietary rights never intended by the patent and trade-mark laws either in this country or in any other civilized country are still going on.

#### CONCLUSIONS.

Proper discrimination is not exercised by the Patent Office in regard to patenting inventions and registering trade-marks. Patents are allowed which should never have been granted. Names are registered as trade-marks with the intention of using them afterward as titles for the purposes of monopoly. During the Great World War it developed that more than 17 millions of dollars worth of patents for synthetic chemicals had been obtained by fraud. Inquiry reveals inadequate facilities and dearth of skilled help at the Patent Office through insufficient appropriations.

Are we to sit by indifferently and permit a group of patent lawyers, "proprietary" manufacturers and advertising firms to establish an international union for the commercial control of the drug business throughout the world?

F. E. STEWART, PH.M., M.D.

#### VISIT TO A BELLADONNA PLANTATION.

It was the privilege of the editor and several friends to visit the Belladonna fields of Messrs. Johnson and Johnson at New Brunswick, N. J., and to observe on a July day many acres of these plants under experienced cultivation. At this time, they were at their best and

in full bloom and the cutting of the tops was in process. In certain fields, plants of two and three years' growth were seen and in others those of the first year. All of these presented a healthy aspect, bespeaking care and the application of scientific methods to prevent the ravages of insects and to obtain the best results in yield and product.

We were equally fortunate in being able to observe the methods used for the extraction of the green herb and of the roots in the laboratory. The Lloyd method of alkaloidal extraction and the Lloyd apparatus for the use and recovery of the volatile solvents being used with satisfactory results.

We appreciate highly the courtesy shown and also the opportunity of inspecting the factory and seeing at first hand the scientific methods adopted by these manufacturers throughout their plant from the purification of the water supply used to the testing, chemically and bacteriologically, of the finished products.

G. M. B.

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## BELLADONNA CULTIVATION IN A PRACTICAL WAY.

BY FRED B. KILMER, PH.M., AND RALPH O. SMITH, PH.D.

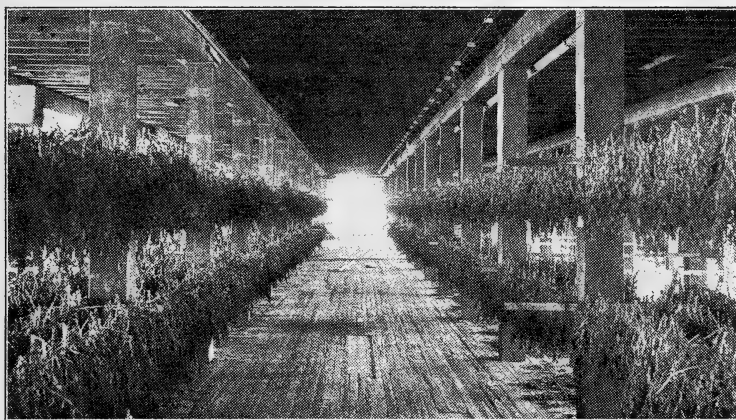
The cultivation of medicinal plants has been urged in the pages of the JOURNAL for a generation. It required a world catastrophe, however, to really quicken interest and place it upon a stable basis. In the earlier period of the war hundreds of growers, either in a large or a small way, embarked in the enterprise without experience and without adequate patience to obtain results. Under these conditions results in many instances were disappointing.

A notable feature of the work has been that the growers who have succeeded were those who approached the problem from an entirely different angle. They were obliged to eliminate the factor of cost, and to solve their problems in a spirit of service, rather than in a spirit of gain. It was necessary to produce drugs, whatever the cost, and they have been produced. It has been worth the effort, and the world has been enriched by the outlay.

The World War caused a scarcity of belladonna, as well as of other drugs, and the culture of this plant has become quite extensive throughout the United States.

The records which follow embrace a summary of belladonna cultivation at New Brunswick, New Jersey, which was begun in

1900, and has continued since that time. In 1919 there were upwards of sixty acres, and there is about the same amount in the field the present season (1920). From these fields we have been pleased to supply seeds for experimental cultivations in various parts of the country, and to give growers the benefit of our experience.



Method of drying belladonna herb by hanging in warehouse.

*Climate and Soil.*—Belladonna can be grown in every State in the Union, and in Canada. It is naturally a shade plant, but it grows well in open localities having cool nights and considerable atmospheric moisture, such as abundant fogs. When well rooted, artificial soil moisture (irrigation) is not essential. When soil moisture is too abundant it is harmful. The plant does not do well in localities where there are long periods of intense sunshine.

Seedlings require abundant soil moisture until they are well rooted. Continued dry weather and sunshine are harmful. When heavy rain is followed by hot sunshine there is apt to be a scalding of the plants, and it is for this reason the ground should be well drained.

In our plantings we have found the plants made slow growth during the hot days of July and August, and that their most abundant growth was during the cool, moist nights in the latter part of August, and in the months of September and October.

The following table gives the mean temperature and rainfall

for this locality during the growing months for the last four years. This climate is not an ideal one for the growing of this plant.

	Precipitation. Inches.				Mean Temperature.			
	1916.	1917.	1918.	1919.	1916.	1917.	1918.	1919.
Apr....	3.52	2.49	3.11	2.73	48.4	48.4	50.0	50.0
May...	3.17	3.87	5.11	5.11	61.6	53.9	65.8	60.7
June...	3.39	3.62	....	5.31	64.7	69.0	67.0	70.2
July...	6.96	6.97	4.54	8.33	74.2	74.0	73.2	73.6
Aug....	2.61	0.87	2.55	6.30	73.6	74.2	75.0	70.3
Sept....	2.53	3.63	3.32	2.01	65.6	61.4	62.7	66.0
Oct....	1.38	7.34	1.30	3.13	55.5	51.4	57.4	60.4

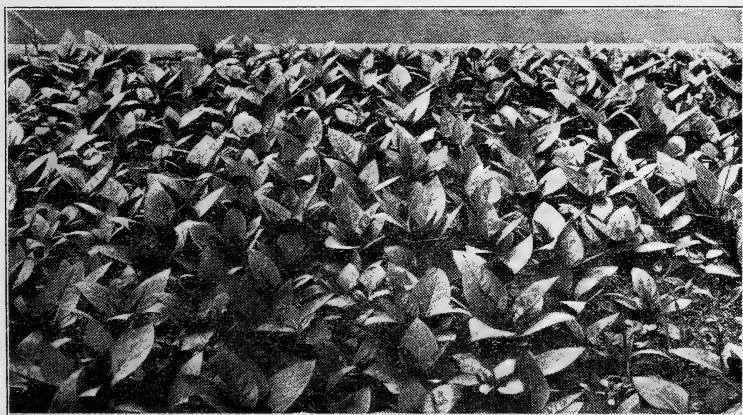
In localities where the frost penetrates deeply into the ground, roots must be taken up in the Fall and protected against freezing, and in turn re-planted in the open ground in the Spring. This is the method which we follow.



Portion of field of first-year belladonna plants. Inset shows an enlarged branch in fruit and flower.

The plant seems to thrive best in deep, well drained, moist loam, with an abundance of lime. After many attempts at soil fertilization, it was found that stable manure was the best fertilizer. Various forms of fertilizer mixtures, such as are used in drug gardens, will increase the growth of the plant, but apparently will have but little effect upon the alkaloidal content.

*Cultivation.*—So far as we are aware, no successful cultivations have been made on this Continent by sowing the seed in the open ground. Seeds of belladonna germinate very slowly. After various attempts to hasten germination by the application of chemical and mechanical measures, we found the most satisfactory method was to sow the seed in the cold-frame in December, and allow them to lie dormant until February. About this time they begin to come through and, if the weather is warm, by April they are ready to transfer to flats. The use of a greenhouse facilitates germination, and the plants are more advanced for transference to the field.



Belladonna seedlings in greenhouse ready for transplanting.

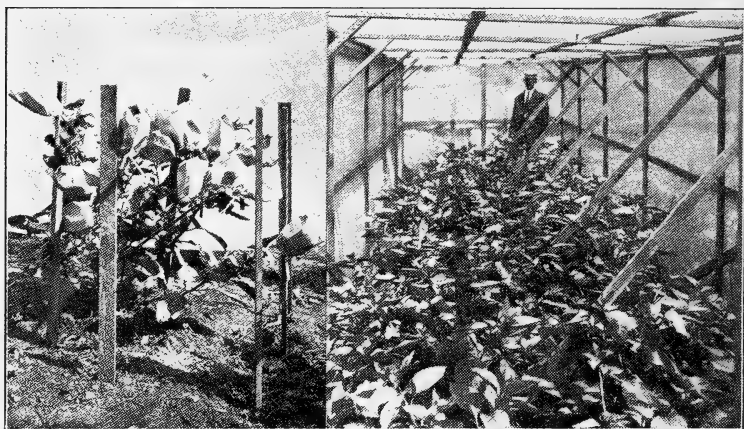
Whether the cold-frame or hothouse method is used, it has been found necessary to transfer the seedlings to flats or pots. While the potting method might be preferable, as giving a more firm root, it entails a greater amount of labor and enhances the cost. (Our potted plants have cost from ten to fifteen cents each.) The seedlings are set out three feet apart, in rows also three feet apart.

Where roots are carried over from one season to another, the problem of placing them in the field is more simple. Here it is only necessary to dig a hole in the ground, and to cover the root to a depth of one or two inches.

In using the roots which have been carried over, the crowns can be divided into from two to five pieces, and each part will give a thrifty plant, especially if large crowns are used. Crowns and

roots are planted more or less like potatoes. The plants are put three feet apart with four feet between the rows.

Cultivation is necessary to keep down the weeds, and to keep the soil fine and well stirred. Irrigation has a tendency to increase root development. If used at all it is only necessary for first-year plants; second- and third-year plants penetrate sufficiently to secure ample moisture. Irrigation increases the tonnage, but not the alkaloidal yield.



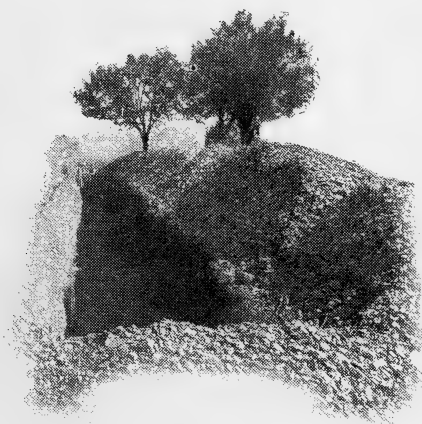
Growing belladonna under canvas shade.

*Harvesting.*—From the first-year plants at least two crops of leaves can be gathered; from second- and third-year plants, two to four cuttings are usual. Harvesting is generally done at the time when the plant is in full flower. At this time the leaves are apt to be the highest in alkaloidal content. To retain the bright green color, which seems to be desirable in the market crop, the leaves should be kept in the shade and dried quickly by the aid of heat. In using artificial heat it is usual to begin with a moderate heat, and gradually increase, some operators reaching as high as 160° F. Other operators have made a great success by beginning a dry process with a high heat—160° F. to 180° F., this for a few minutes only, then the leaves are passed through a moderate heat. This completes the process.

In California they are able to dry the leaves in the sun. In our locality we meet with rain and lack of sunshine sufficient to prove disastrous.



When the leaves and stems are to be used they can be dried in a manner similar to tobacco, but under this condition the leaves will turn brown. The demand for the bright green color in the leaves of belladonna, and other plants, seems to have no valid reason, except custom. The presence of a high content of chlorophyl in pharmaceutical preparations is at times embarrassing.



Trench in which roots are buried for protection against frost.

A very acceptable supply of herb can be secured by a process of "curing," which eliminates the green color, and gives a fairly uniform product of a brown shade.

In gathering roots they are usually plowed from the ground late in the Fall. The larger roots are split, and they are then washed and dried.

In all parts of the country belladonna has been reported to have been attacked by many forms of disease, and by insects. In the early years of our work potato bugs and other species of insects were very troublesome; later the plants seemed to acquire a resistance to insect enemies.

During very hot days the lower leaves of the plant, near the ground, are often killed by the sun's rays. Spring frosts will kill off the leaves and young shoots and, if severe, may be disastrous to the entire plant.

*Yield.*—The yield of leaves and stems is greatest in the second- and third-year plants. The roots and stems of old plants are apt

to become woody and fibrous, with a decrease in the quantity of alkaloid.

Stockberger reports the results obtained from sixty growers of belladonna for 1917, as approximately 600 pounds of belladonna herb, and 164 pounds of root per acre. Reports have been made of first-year plants where two cuttings of the plant yielded 1300 pounds of herb, dry weight, and where second-year cuttings of the herb yielded over one ton, dry weight.

In our work we have estimated our results upon the yield for the season per thousand plants, rather than by acreage. Our estimates are made on the weight of the plants in their green, or undried, state.

#### HERB YIELD PER THOUSAND PLANTS (GREEN).

Second-year plants.	Lbs.
Herb.....	1177
Alkaloid.....	0.891
First-year seedlings (potted plants):	
Herb.....	527
Alkaloid.....	0.313
First-year seedlings (cold-frame plants):	
Herb.....	534
Alkaloid.....	0.289

From this showing the greatly increased yield of plants in the second year is manifest. It is also shown that the potted plants from the greenhouse give but a slightly larger yield. The loss of moisture during air drying, based upon the entire crop of herb, averaged 84.07 per cent.

#### ASH IN AIR DRY DRUG.

##### *Herb.*

	Highest Per Cent.	Lowest Per Cent.
Three year old plants.....	13.15	8.62
Two year old plants.....	17.53	11.68
First-year seedlings (potted).....	14.47	10.10
First-year seedlings (cold-frame).....	17.54	12.77

##### *Roots.*

Three year old plants.....	8.97
Two year old plants.....	15.09
First-year seedlings (potted).....	7.88
First-year seedlings (cold-frame).....	8.81

##### *Whole Ripe Berries.*

From three-year old plants.....	4.04
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The limit of the U. S. P. for belladonna leaves is "not more than 20 per cent. of ash"—for belladonna root "not more than 7 per cent. of ash."

The standard suggested by the American Drug Manufacturers' Association for belladonna herb is "not more than 18<sup>7</sup> per cent. of ash."

These standards may need to be changed to meet the condition of cultivated belladonna, especially so when cultivated upon soils containing a considerable content of lime and potash.



Belladonna seedling, pot grown.

*Cultural Experiments.*—Concurrently with other growers, we have attempted to increase the alkaloidal content of belladonna. The experiments have shown that the use of lime is a possible factor. It is well known that in England chalk soil is particularly adapted to the growth of this plant.

Attempts have been made to take advantage of the great variation in the alkaloidal content in individual plants, with a view of developing plants high in alkaloid, either from the seed or crown of those plants which ran high in alkaloidal content. Work of this character is surrounded with great difficulties. It has been found that a slight variation in the condition of growth would cause a marked change in the characteristics of the plant. Only in rare instances would the seeds or crowns carry forward the characteristics of the parent plant. Cross-fertilization between plants high

in alkaloid has brought no tangible results. For the most part plants will breed true only for two or, at least, three generations. So far as our knowledge goes, no hardy strain of belladonna has been developed. Experiments of growing under shade, such as tobacco cloth, while giving a somewhat increased yield, were not sufficiently striking to warrant a continuous use. A number of growers have produced a strain which gives a large leaf.

The Department of Agriculture at Washington has, in a small way, produced a strain of belladonna which will give a larger yield of alkaloid in the leaf and stem, and they are hopeful that this character may be transmitted.

*Belladonna Herb.*—Growers of belladonna are severely handicapped under present conditions, whereby the leaves and the roots only are marketable.

The Ninth Revision of the Pharmacopoeia required that belladonna folia should be "without the admixture of more than ten per cent. of stems or other foreign matter." Under this standard the grower is deprived of the sale of from thirty to fifty per cent. of the tops.

The relative weights of green herb and root from typical plants is shown by the following figures, which were secured from two or three plants of each lot designated, selected at random at the close of the season. These plants had, of course, yielded from two to four cuttings earlier in the season:

#### COMPARATIVE YIELD IN HERB AND ROOT (GREEN)

Three year old plants:		Per Cent. Alkaloid.	Grams Alkaloid.
Herb	1744 grams.....	0.083	1.45
Roots	1188 grams.....	0.163	1.94
First-year seedlings (potted plants):			
Herb	1144 grams.....	0.061	0.70
Roots	548 grams.....	0.159	0.87
First-year seedlings (cold-frame plants):			
Herb	1079 grams.....	0.062	0.67
Roots	466 grams.....	0.167	0.78

Numerous authorities have shown that the stems of belladonna equal, and at times exceed, in alkaloidal content the standard of the Pharmacopoeia. Our work has repeatedly shown that the whole of the stems of the plant can be mixed with the leaves—in other words, the entire tops of cultivated belladonna—and fully meet the alkaloidal requirements of the Pharmacopoeia.

Strong efforts are being made to stimulate the cultivation of drugs in this country. To accomplish this every inducement must be made in behalf of the grower. With belladonna, and many other drugs, it may be necessary to revise our standard, the more especially so when such revision does not in any way detract from the medicinal value of the drug.

In respect to belladonna, the American Drug Manufacturers' Association has suggested that belladonna herb, by which term they intend to include the dried leaves and stems, should be made official in the Pharmacopoeia, and allowed to be used for galenical preparations in the manufacture of medicinal products. They suggest that belladonna herb should be inserted in the Pharmacopoeia in addition to belladonna leaves and belladonna root.

Our records for the year 1919 show that the tops of belladonna, including the stems, would fully meet the requirements of the Pharmacopoeia.

The following figures are taken from the records of herb cut from three to six inches from the ground, without any attempt at selection, at such times as we found convenient for gathering, and without any particular reference to the alkaloidal content. This latter for the reason that the drug was to be made into assayed products.

BELLADONNA HERB (AIR DRY STEMS AND LEAVES)—1919.

Plot Number.	Per cent. alkaloid.	
	Highest.	Lowest.
1—500 three year old plants.....	0.491	0.385
2 and 5—50,000 first-year seedlings (potted plants).....	0.473	0.328
7—33,000 two year old plants.....	0.570	0.392
8—1,600 three year old plants.....	0.524	0.520
10—72,000 first-year seedlings (cold-frame).....	0.515	0.305

From the foregoing it will be seen that the entire crop from this 150,000 plants, taken separately or mixed together, would at all times have exceeded the requirements of the Pharmacopoeia, and there would therefore seem to be no good reason why belladonna herb, especially that obtained from cultivated plants, should not be admitted to the Pharmacopoeia under proper restrictions as to alkaloidal content, etc.

*Conclusion.*—Much progress has been made in the growing and collection of belladonna in the United States. We are no

longer dependent upon foreign sources for such drugs as can be grown in our climate.

We have not yet reached the point where production can be made on the pre-war basis as to cost. In some of the earlier work here outlined, belladonna herb and root cost ten dollars per pound, and owing to labor and other conditions the cost is still high.

There are numerous advantages in the home source of supply for drugs. These include the securing of a higher and more uniform quality from the cultivated plant, and the fact that the drug can be grown, gathered and utilized under scientific control.

Many problems yet remain unsolved, and to these the pharmaceutical worker may well give his attention.

The cultivation of drugs should continue to receive the fostering care of the government, the manufacturer, the dealer, and the dispenser of medicinal preparations.

Wherever possible the standards should be revised, so that we may reap the full benefits to be derived from the American grown supply.

RESEARCH LABORATORY,  
JOHNSON & JOHNSON,  
NEW BRUNSWICK, N. J.

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## METHYL ALCOHOL AND ETHYL ALCOHOL: THEIR SOURCES, MANUFACTURE AND USES.\*

BY H. R. FRENCH.

### METHYL ALCOHOL.

As Wood, or Methyl Alcohol is in such strenuous demand to-day for many manufacturing purposes, owing to the fact that it is the only satisfactory natural source of the methyl, or  $\text{CH}_3$  radical, for the manufacture of Methyl Aniline Dyes, which dyes are the principal blue colors, the manufacture of Methyl Salicylate or artificial Oil of Wintergreen, and the manufacture of moving picture film, in which it is used as a solvent, I will treat this subject first.

The destructive distillation of wood is one of the most important of industries. Its economic importance is also great, as wood distillation provides for the utilization of wood waste, and what in

\* Read before the meeting of the New Jersey Pharmaceutical Association, Newark, N. J., June, 1920.

years gone by was allowed to decay upon the ground may now be converted into substances necessary and useful to all mankind. No one knows exactly when wood first began to be carbonized and it probably dates back to the beginning of civilization.

At first, however, and even up until approximately a century ago, charcoal was the only by-product obtainable, and it was not known that the vapor, which passed out into the air as "smoke," contained valuable elements which would some day play an important part in the affairs of the world. From the primitive method of burning charcoal in pits to the modern tubular condenser has been a long stride. The tubular condenser is equipped with vertical copper tubes set in specially made tube sheets and surrounded by water contained in a steel tank. The vapor dome and liquor receiver are of copper and a copper trap is provided at the outlet, so that the non-condensable gas may be piped off to be used as fuel. This condenser represents the results of years of research and experience and its high efficiency is a distinguishing feature.

*Equipment and Method of Distillation.*—Modern hardwood distillation plants are equipped with oven retorts which insure economy, efficiency and surety of operation so essential to the success of the business. In the employment of ovens, the wood to be carbonized is loaded on cars and no further hand labor is required in connection with it, as the cars convey it into the ovens, where it is carbonized, and the resultant charcoal, still on the same cars, is carried through a succession of coolers and sheds, finally arriving at the point where it is transferred to bins or to railroad cars for shipment. Even in this last transfer, hand labor has been reduced to a minimum by the use of some of the modern charcoal unloaders.

*Cars.*—The first step in the process of distillation is to load the wood on cars. These are made especially for the purpose and are all of steel construction, except the wheels and drawheads, which are of cast iron. The bottom, sides and ends are made of steel bars, securely riveted in place. The sides are quickly detachable to provide for easily loading the wood and unloading the charcoal. The frame is rigidly made of structural steel members, thoroughly braced and securely riveted together. The wheels revolve on specially made bearings, so that the cars are comparatively easy to move. After being loaded with wood the cars are placed in front of the ovens. An oven of 10 cords capacity holds four cars to a charge, and these are placed in a line, all together, on the track lead-

ing to the oven. All the ovens in the plant have the cars so placed before them, usually some little time before the cars are actually run in, so that the ovens may all be recharged, one after another, without the loss of time between. After the cars have been placed in the ovens, the doors on the ovens are closed and the process of carbonization is begun.

*Ovens.*—Ovens are of varying sizes, from 1 to 10 cords capacity, and usually have a door at each end, so that cars may be run straight through, thus obviating the necessity of turn-tables or transfer tables. Their construction is very strong and rigid. Steel hangers are riveted to the sides, and each hanger is supplied with shackle, U-bolt and suspension washer, the purpose of the hangers being to allow the oven to expand and contract without restriction. Inside of the oven, there is a track for the cars to run upon, and this is made so that it can expand and contract independently of the expansion and contraction of the oven itself. The doors and frames are of cast iron, while the remaining portion of the oven is of steel.

The doors are hinged and when closed are held in place with tapered keys, which are easily inserted and easily withdrawn. The door joints are tongued and grooved and made tight with asbestos packing. They are set in pairs and are bricked in. There is a smokehood to provide egress from the building of smoke and gases which issue from the oven when the discharge end door is open, and the cars are being pulled out. One smoke stack is required for two ovens, and this is placed in the center of the setting. Ducts are provided in the brick work to properly convey the smoke into this stack. Dampers are furnished to give desired control, and individual control of each oven may be had. There are clean-out doors on the sides of the settings, both below and above the ovens. Above the ovens is a drying floor.

*Carbonizing Process.*—It requires from 18 to 24 hours to carbonize one charge of wood in an oven retort. During this period, the fires in the furnaces are kept burning continuously, but the temperature is allowed to gradually rise from the beginning of a charge to its maximum point, which is reached from six to eight hours after the beginning. Then the maximum temperature is maintained for a variable period, and finally the furnace fires are allowed to go down and the temperature in the ovens gradually decreases until the end of the run. The latter end of the distillation is accomplished by the latent heat in the ovens and their settings.



In from one to two hours after the wood is placed in the ovens, water distillation takes place, and this distillate has an acid content of about 2 per cent. The next to issue from the wood is called "green gas," and this comes freely for about five to six hours. At about 300° Fahrenheit the endothermic reaction begins, but it is more decided at the maximum temperature, which is about 680° Fahrenheit, and at this latter point great care must be exercised that the liquor is not "burned;" that is, the temperature must not be permitted to rise higher, otherwise there will be an undue formation of condensation products. After the wood has been in the heating process for about six hours, the temperature attains an average of about 450° Fahrenheit. About the sixth hour pyroligneous acid begins to flow from the condensers and continues up to about the eighteenth hour. The color of this acid determines whether too much heat is being maintained and whether the wood fibers have been broken down sufficiently. At the latter end of the heating process the distillate forms a considerable portion of tar.

*Charcoal Coolers.*—The cars, now containing the charcoal, are drawn out of the ovens and into the first coolers, where they remain for a period of about 24 hours, or the length of time required to carbonize the wood in the ovens. The cars are then moved into the second coolers, where they remain an equal length of time. These coolers are similar in shape to the ovens, are made of steel and are equipped with two doors, one at each end, so that the cars may be run straight through. The coolers are placed in line with each other and with the ovens, and are at the discharge end of the ovens. Coolers are not so heavy in construction as ovens, because their purpose is to radiate the heat from the charcoal and dispose of it in the air. A small vent is provided in each cooler for the vapors to pass out, yet this vent is not large enough to allow much oxygen to enter. The function of the coolers is to prepare the charcoal so that it may be exposed to the air. If the hot charcoal should be taken out of the ovens and left standing in the air, it would immediately ignite from spontaneous combustion. Therefore, it is drawn into the coolers, where it can stand without being exposed to the air, and gradually its heat passes off through the steel of the cooler.

*Charcoal Sheds.*—After leaving the second coolers, the cars of charcoal must stand in the open air under shed roofs for a period of 48 hours. This is a requirement of the government to insure that there is no danger of spontaneous combustion. After that

time, it may be loaded in freight cars for shipment, but it must be left standing in these cars for at least twelve hours before shipping. Before such precautions were taken, many fires took place and many railroad cars were destroyed.

*"Raw" Liquor.*—The vapor which issues from the vapor outlet nozzles of the ovens and which passes off from the wood during the process of carbonization enters tubular condensers and is converted into a liquid called pyroligenous acid, or "raw liquor." This does not come from the condensers during the entire period of carbonization, but only from about the sixth to eighth hour on to the end of the run. It is a yellowish green, ill-smelling liquor during most of the run, and towards the latter part its color changes and becomes quite dark. This acid is collected from the condensers by means of a copper branch into a main copper pipe line which passes through the middle of the retort setting and terminates in a wooden sump set in the ground. These sumps are simply for the purpose of providing a reservoir into which the raw liquor may be run.

*Gas.*—The oven vapor is not all condensable, but one of the products of distillation is wood gas, termed by the manufacturers "non-condensable" gas. This is trapped off at the outlets of the condensers and used for fuel. It has been found that about 11,000 to 14,000 cubic feet of this non-condensable gas are obtained from each cord of wood distilled, and has a considerable value. It is carried from the condensers in copper pipes into a main gas line, and there are also copper distributing lines to convey it to the oven furnaces and to the boilers.

The raw liquor is pumped from the sumps to a series of wooden settling tanks. The pump used for this purpose must be entirely of brass, or brass lined. The brass construction is necessary where the liquor comes in contact with the metal, as the liquor is acid and therefore the metal must be acid-resisting.

*Wooden Settling Tanks.*—The purpose of these tanks is to allow the tar in suspension in the raw liquor to precipitate. The tanks are so connected together that the liquor passes from one to the other serially, and the pipe connections between them are at varying heights, the connection to the first tank being high up, and the other connections being made gradually lower down, until the connection in the last settler is only about one-third of the distance above the bottom. The first settler accumulates the most tar

and each of the others less than the preceding one, which is the reason for the varying heights of the connections.

*Tar Still.*—The tar in the bottom of the wooden settlers is drawn off and collected and then refined in a wooden tar still equipped with a copper steam heating coil and with a copper tubular condenser. The wood oils are recovered by means of this still. The tar residue left in the still is conveyed to the tar storage tank to be used as fuel.

*Primary Still.*—The liquor in the last of the wooden settlers, which is practically free from tar in suspension, is run by gravity through a copper pipe into a copper primary still, and the feed is continuous and kept so by a float valve. In this still the tar in solution is separated. The still is made entirely of copper and supplied with a copper steam heating coil, copper neck and copper tubular condenser. The tar from the primary still is considered a waste product and is conveyed to the tar storage tank to be used as fuel.

*Neutralizing.*—The liquor which is obtained by the condensation of the vapor issuing from the primary still and passing through the condenser is conveyed to a wooden neutralizing tub, where it is treated with slaked lime. The tub is provided with an agitator to properly carry on the neutralization.

*Lime Lee Still.*—The neutralized liquor is carried to a steel still, called a lime lee still, and here the acetate of lime is separated from the wood alcohol. It is equipped with a copper steam heating coil and with a copper tubular condenser. From the lime lee still the process separates into two branches.

*Settling Tanks and Steam Pans.*—We will first follow the progress of the acetate solution, which is what remains in the lime lee still after the wood alcohol has been driven off in the form of vapor. The acetate solution is pumped or blown with steam or compressed air from the still into steel settling tanks, in which the solid matter precipitates. The solution is then drawn off and piped into steam-jacketted evaporating pans, where the greater portion of the water is evaporated, leaving a substance of consistency which can be handled with an ordinary hand shovel. From these pans the substance, which is acetate of lime, is shoveled out onto drying floors situated above the ovens, and it is spread in a thin layer and allowed to become thoroughly dry. This is now grey acetate of lime of an

average of 80 per cent. and is ready to be placed in bags for shipment.

*Drying Floors.*—The drying floors are over the tops of the ovens, and are made of tile brick or concrete. They are supported by I-beams or rails and are so designed that they utilize the waste heat above the tops of the ovens.

*Weak Alcohol.*—Returning to the lime lee still, the vapor which passes off when the contents are heated goes through a tubular condenser and the condensation product, termed weak alcohol, is conveyed into steel tanks, the capacity of which is sufficient to supply one charge for the alcohol still.

*Alcohol Still.*—The weak alcohol is piped from the tanks just mentioned to a steel alcohol still, equipped with a copper steam heating coil and with a copper fractionating column. Its purpose is to remove the water from the solution and to produce 82 per cent. wood alcohol (called crude alcohol), which is the grade manufactured in most of the wood distillation plants.

*Woods and Yields.*—The principal kinds of hard woods used in destructive distillation are beech, birch, maple, oak, hickory, red gum and others which are comparatively free from gums, tannins, etc. Any part of a tree can be used down to the branches two inches in diameter. The wood is allowed to season for several months before being carbonized, the idea being to allow nature to remove as much as possible of the superfluous water in the wood. Different kinds of woods yield different quantities of by-products, the average, it is said, being about as follows for each cord of wood: Charcoal, 50 to 60 bushels; acetate of lime, 190 to 240 pounds; 82 per cent. wood alcohol, 9 to 12 gallons. Charcoal weighs approximately 20 pounds to the bushel.

The crude wood alcohol is taken from the alcohol still of the crude wood plants, and shipped to wood alcohol refineries, the principal ones in the United States being located in Buffalo, N. Y., and Newark, N. J. Here the crude alcohol is first pumped into storage tanks, and after careful analysis, showing the amount of alcohol, amount of acetone, and amount of oils present, it is drawn into big iron stills, where it is treated with an amount of caustic soda, sufficient to take care of oils and impurities indicated by the analysis.

After this reaction has had an opportunity to proceed to the right point, it is distilled, the distillate being water-white and gath-

ered in large tanks. This is then drawn into copper stills where it is treated with sulphuric acid to neutralize any alkaline bodies which may have been carried over in the distillation on caustic soda treatment, and is then carefully distilled in column stills.

The first part of the run contains acetone and esters figured as methyl acetate. Methyl acetate is one of those peculiar organic bodies which has a high specific gravity and exceedingly low boiling and volatilizing point. This mixture of acetone, methyl acetate and alcohol, which is first fractionated off, is sold under the trade name of Methyl Acetone, and is used largely as a solvent.

Next is fractionated off that part of the run which is pure alcohol, containing, when carefully watched, less than  $\frac{1}{10}$  of 1 per cent. acetone, and being as near pure chemically into  $\text{CH}_3\text{OH}$  as is possible to obtain. This is the part used by the formaldehyde and dye manufacturers.

The last part of the run, or tailings, so-called by the distiller, contains some very accurate poisonous compounds, and this is the portion used for making denaturing wood alcohol, which is the material specified by the Internal Revenue Department for the denaturing of ethyl alcohol.

*Uses of Wood Derivatives.*—The chemicals derived from the destructive distillation of hard woods are used as follows:

Uses of Charcoal:

In the manufacture of charcoal pig-iron; in the manufacture of gunpowder; artificial fertilizer; insulator; deodorizer; metallurgical purposes; briquetted fuel; domestic lump fuel.

Uses of Acetate of Lime:

Acetic Acid—For manufacturing acetates, artificial vinegar and in photography, tanning, dyeing, and the curing of skins.

Acetone—For manufacturing gunpowder, chloroform and iodoform; also in the paint trade as a solvent.

Aluminum Acetate—For dyeing, mordanting and waterproofing fabrics.

Chromium Acetate—For mordanting cotton.

Copper Acetate (Verdigris)—Used for oil paints, green colors, artificial flowers, stains for wall paper and for dyeing black on wool.

Iron Acetate—Used for impreganting wood, dyeing black and violet, dyeing and weighing raw silk, and in the manufacture of hats and inks.

Lead Acetate (Sugar of Lead)—In painting, calico printing, loading white silk and in the manufacture of chrome yellow and thirty derivatives therefrom.

Potassium Acetate—In the manufacture of acetic acid and of dehydrating and decomposing agents.

Sodium Acetate—Same as in preceding paragraph.

Uses of Wood Alcohol:

For denaturing grain alcohol, in the manufacture of gunpowder, manufacture of aniline coal tar colors, manufacture of formaldehyde, manufacture of celluloid and moving picture film, and as a solvent for hydrocarbon resins and gums. Shellac made from wood alcohol being very much superior to any other.

So great has become the demand for wood alcohol, and there has been so little increase in supply, that prices have risen in the last few years from 40 cents to 50 cents a gallon to \$3.00 to \$3.50 a gallon, owing to the grade, and even at these prices it is impossible to supply the demand.

#### ETHYL ALCOHOL.

Ethyl, or so-called grain alcohol, in which the drug trade are most vitally interested, has been for the past several years, owing to high price of grain, made practically entirely from molasses. The molasses used is what is known in the trade as black-strap molasses, and is the final residue after all the sugar has been crystallized out of the concentrated syrups from whatever source the sugar may come. This molasses is taken to the distilleries in tank steamers, or tank cars, and in some instances by pipe lines, where it is conveyed by pipes into big fermenting tubs.

In these tubs it is mixed with just the right amount of water and yeast, cultured. After fermentation has been allowed to go to just the right point, which an expert can detect by watching the action closely, the mixture is drawn into a big still, known as a beer still. Steam is immediately turned on, and the alcohol in crude forms is distilled over.

This alcohol is then treated, first with alkali, giving primary distillation similar to that of wood alcohol, and then neutralized with acid, and redistilled in a column still.

The first alcohol that comes over has some odor, and is not over 188 proof. The next alcohol is the heart of the runs, which runs 190 to 192 proof, and is entirely free from odor, and is what is known

in the trade as Cologne Spirit. The last of the run develops some odor again, and contains aldehydes which, for many chemical purposes, cause disastrous results.

For pharmaceutical uses and for chemical uses, the heart of the run, or what is known as Cologne Spirit, is all that is fit to use. The first of the run, which is called the heads, and the last, which is called the tails, are mixed together to be used for ordinary denatured alcohol for non-freezing and solvent purposes.

The Internal Revenue Department has permitted a number of formulas of Denatured Alcohol aside from those which are authorized for Completely Denatured Alcohol, that can be sold to anybody. These additional formulas are known as special formulas, and can be bought by any manufacturer who has sufficient responsibilities to secure bond. Bond must be given for the amount of tax that this said manufacturer would be liable to, should this alcohol be misused. In other words, the manufacturer must give bond enough to cover \$4.18 a wine gallon for every gallon of alcohol which he uses, or has on hand during a period of 30 days.

A number of these formulas are particularly applicable to pharmaceutical preparations, but it must be definitely understood that they are only to be used for the purpose for which they are specified, and in no instance are they to be resold, except as the finished product for which they are intended.

Since the first of the year, alcohol prices have mounted to the highest levels on record. Sales of spot ethyl alcohol, 190 proof, have been recorded during the past month at figures ranging anywhere from \$6.00 per gallon up to \$8.00, which prices consumers have been compelled to pay, buying in a resellers' market. For shipment from middle western or southern distilleries, goods have been offered at \$5.40 up to \$5.75, but with the present railroad situation, the actual time of delivery to the consumers' plants makes this a rather uncertain type of purchase. Contracts in effect between distillers and consumers at the present time are understood to be priced at slightly over \$5.00 although a contract is said to be no assurance of obtaining a steady supply of alcohol to-day. The fact that many large users have been forced into the open market to pick up spot alcohol in any way that they have been able, is evidence of the general shortage of supplies.

*Causes of Shortage.*—In speaking before an association of one of the leading consuming industries in the country, the president of a

large producing corporation said recently that supplies of alcohol all over the United States were far below normal and that he could not see at the time from what source legitimate consumers would be able to obtain sufficient supplies for their needs after the present short holdings are used up. Distilleries using molasses as a raw material have been unable to obtain anything like enough to keep them running at capacity. For those using corn, which is now just under the two dollar mark, the price has become almost prohibitive. Added to this, practically two months of crippled shipping facilities have furnished the crowning feature of the situation by isolating consumers from their sources of supply and holding up shipments of raw materials destined for the distilleries.

The molasses production of Cuba, from whence comes most of that used in this country for the production of molasses alcohol, has been materially curtailed during the past year by strikes. The high price of sugar has also been a factor in the more careful refining which has given a higher sugar return and consequently reduced the molasses output. The market and prices in the United States have been on what is termed a "grain basis" as a result, that is, the cost of alcohol corn has been the determining factor in the price and is expected to be for the balance of this year if not longer. The present price of corn for alcohol (about \$1.60 per bushel) means a cost to the producers of 70 cents to 75 cents a wine gallon.

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SUGGESTIONS FOR UNITED STATES PHARMACOPOEIAL  
REVISION SUBMITTED BY THE COMMITTEE ON  
THE UNITED STATES PHARMACOPOEIA OF THE  
PHILADELPHIA COLLEGE OF PHARMACY.

MAY, 1920.

(Continued from p. 563, August, 1920.)

BIOLOGICAL PRODUCTS AND STERILIZATION.

*Aqua Destillata Sterilisata*.—Mention should be made here, as under physiological solution of sodium chloride, that an autoclave is to be preferred for its sterilization. When boiling is to be used, the term "actively boil" should be employed, and not merely boil. The statement is made that this preparation should be used within forty-eight hours after it is made. This should be followed by the statement, "if it is to be used for intravenous injections." It is



neither necessary nor practicable to use a freshly prepared product except for intravenous or intramuscular injections.

*Liquor Sodii Chloridi Physiologicus.*—In the sterilization of this preparation, boiling is permitted for at least one hour, but no mention is made of the fact that if such a process is used, the evaporated water must be replaced by sterilized, freshly distilled water. Such a statement should be inserted, and the operator directed to simultaneously prepare sufficient sterilized, distilled water in a second flask. In stopping the flask, it is desirable to place a piece of sterile gauze under the cotton plug.

The statement is made that this solution should not be used after it has been made forty-eight hours. This should be followed by the phrase, "if it is to be used for intravenous injections."

Why should sterilized distilled water be boiled for one-half hour and this preparation for one hour to insure sterile end products? For the sake of uniformity, the time directed should be the same in each case.

*Virus Vaccinicum.*—Mention is made that the pulp is rubbed up into a smooth emulsion with glycerin. It might be well to state, "with sufficient glycerin to cause it to conform to the established standard."

*Blood Coagulants.*—There is a large demand for a good blood coagulant. A method of preparing such a product, together with a method for its standardization should be introduced into the next U. S. P.

*Beef Extracts*, page 527.—Why should the U. S. P. refer to Liebig's or any other make? It is true that this make is very satisfactory, but the Pharmacopoeia should not name any specific manufacture.

#### REAGENTS, TEST SOLUTIONS, ETC.

*Culture Media.*—If retained, a more comprehensive list should be included. Methods for determining reactions or, if advisable, the hydrogen-ion value of these products should be added.

*Sterilization.*—A page and a half is devoted to the exceedingly interesting and important subject of sterilization. A more intensive and instructive chapter, giving the specific details of procedure should be provided. As it is at present, it is of little value and might as well be deleted.

*Staining Solutions.*—If retained, mention should be made of Pappenheim's Solution and Aniline Gentian Violet, giving the ingredients and methods of preparation.

*Blood Reaction, page 619.*—The benzidene test should be introduced.

*Urea Estimation, page 620.*—The Urease Method for determining urea should be introduced.

*Benedict's Solution, page 621.*—These solutions for qualitative and quantitative determination of glucose should be introduced. Mention should be made of the fermentation method for the determination of glucose in urine.

*Gastric Contents, page 621.*—Sahli's reagent for the determination of free acidity should be mentioned, as well as Uffelmann's reagent for lactic acid.

*Diagnostical Reagents.*—If the Revision Committee decides to retain the Diagnostic Reagents in the U. S. P., many other reagents which are at present used in the Newer Blood Chemical Tests should be introduced. In making up such tests, there are also standard solutions for colorimetric comparisons, in addition to reagents, which it is desirable and essential to include in the Pharmacopoeia.

#### PHARMACODYNAMICS.

The incorporation of the chapter on "Biologic Assays" in the U. S. P. IX is an epoch in the history of standardization and this method of assay should be applied to a greater number of drugs which cannot be satisfactorily assayed by chemical means.

We recommend that more of the methods be made compulsory instead of optional and that biologic assays be included for Ergot, Gelsemium, Lobelia, and Veratrum Viride. We would, however, recommend that these tests be referred to as "Pharmacodynamic Assays" instead of "Biologic Assays", and thus make the Pharmacopoeia conform with the definitions of the Pharmaceutical Syllabus.

As a result of personal experience and the number of papers which have been published criticising the present U. S. P. methods, we are of the opinion that the "Biologic Assay Methods" of the U. S. P. IX are unsatisfactory, due to the fact that in many cases *they lack the details* which workers in the practical laboratory have found essential in order to obtain accurate results. In other words, the methods are in many instances *not as accurate and up-to-date* as the methods in common use at the present time in commercial

laboratories, and therefore do not show as well as they might, the degree of efficiency to which biologic assays have been developed.

Due to this fact, very little attention has been paid to the methods as set forth in the U. S. P. IX, as all evidence tends to prove that they are less accurate and reliable than the methods in common use.

In the second paragraph of the chapter on "Biologic Assays" in the U. S. Pharmacopoeia, the following statement appears:

"Brief descriptions of the more commonly accepted methods are given here in order, first, to direct the attention of manufacturers to them; second, to ascertain the points of weakness which may exist in them; and, finally, to outline methods and establish standards which those interested may adopt should they desire to assay their products and have them conform to the standards proposed."

For the reasons stated above, remarks are mostly limited to what we consider "points of weakness" which exist in the present U. S. P. methods.

*Cannabis*, page 605.—"Before administration the animal should not be fed for twenty-four hours in order to hasten absorption."

It is not necessary to withhold food for more than ten to twelve hours before making a test, as the stomach will be completely emptied in this time and it will not be so hard on the animal.

"The head of the animal being held, its mouth is opened and the capsule or pill is placed upon the back of the tongue. Usually the drug is easily swallowed when given in this way, but this may be facilitated by giving the animal a small amount of water to drink."

This method works sometimes, but as a general rule the dog does not feel inclined to take the capsule so easily. In practical work it will be found that it is almost impossible to make the dog swallow a capsule by the above method. Pulling the tongue well forward, placing the capsule far on the back of it and then releasing the tongue, is an improvement, but the best method is the following:

"Open the animal's mouth by forcing the thumb and index finger of the left hand between the jaws, back of the teeth. The capsule is then placed on the back of the tongue with the right hand and the mouth quickly closed; while still holding the mouth shut, the animal can be made to swallow the capsule immediately by slapping it on the throat."<sup>1</sup>

By this method the most obstinate dog can be made to swallow the capsule on the first attempt.

<sup>1</sup> Pittenger: "Biochemic Drug Assay Methods," page 101.

In lieu of a standard extract furnished by some central authority such as the U. S. Hygienic Laboratory, what is the use of running an assay each time on a standard preparation when the strength of the standard is obtained by adjusting a preparation until it is of such strength that 0.03 Mil. of the fluid extract per kilo will produce incoördination.

Why not adopt 0.03 Mil. per kilo as a standard and calculate the strength of the unknown by comparing the dose of it necessary to produce incoördination with the above 0.03 Mil. per kilo instead of the amount of the standard necessary to produce the same effects? If the standard is of proper strength, will it not require exactly 0.03 Mil. per kilo? The only object for assaying the standard preparation each time would be to avoid errors due to the variation in the susceptibility of dogs. The use of a standard preparation, unless supplied by some central authority, will not avoid this error because the standard preparation is adjusted to the above *standard dose* and not to *standard dogs*. Are you not just as liable to have dogs which are over or under normal susceptibility when you adjust the standard as when assaying an unknown, thus making the standard slightly over or under strength? If so, by adopting the longer process of assaying both standard and unknown each time, the error due to variation in susceptibility is only increased because you adopt as a standard preparation one which may be slightly over or under strength and then adjust all subsequent preparations to this, thus making the same error in all, whereas by the shorter method of adopting a definite dose as standard we only have an occasional preparation a little off strength, due to an over or under susceptibility of the dogs used on that particular assay.

Due to the variation in susceptibility of different dogs, the method must essentially be comparative and not absolute. This necessitates the adoption of an arbitrary standard with which the activity of the unknown can be compared. The U. S. P. method would, therefore, be very satisfactory had the Committee only gone a step farther and, as suggested by Pearson,<sup>1</sup> made arrangements for supplying manufacturers with a suitable standard with which to compare the activity of their preparations. Until such a standard is supplied, however, it is only a waste of time to run an assay on a standard preparation, *which the manufacturer has prepared himself*; each time an unknown sample is tested.

<sup>1</sup> Pearson, THIS JOURNAL, Nov., 1916.

Some workers have objected to the standards adopted by the Pharmacopoeia for Cannabis, claiming that they are too high. Personally we have found no difficulty in meeting the U. S. P. requirements for preparations of Cannabis.

The method of stating the standard, however, is open to criticism. The U. S. P. states:

"When assayed biologically Fluid extract of Cannabis produces incoördination when administered to dogs in a dose of not more than 0.03 Mil. per kilogram of body weight."

According to the above statement, a dose larger than 0.03 Mil. per kilo would not produce incoördination. The words "not more than" should either be omitted or changed to "in a minimum dose of 0.03 Mil. per kilo."

Some workers have objected to the action of the Committee in making the test for Cannabis compulsory because it is one of the least satisfactory of the pharmacodynamic tests, and would, therefore, be a hardship on the retail druggist in that he would be held accountable for the activity of his Cannabis preparations when only an expert could satisfactorily carry out the test.

This criticism would be justified had the Committee adopted a standard reading "the minimum dose of Fluid extract of Cannabis necessary to produce incoördination should be *not less than* — Mils per kilo, nor more than — Mils. per kilo."

The standard adopted, however, only specifies a *minimum* activity in order to guard against fraudulent, inert or badly deteriorated drugs and does not specify "limits" as in the chemical assays for alkaloidal drugs.

No hardships are imposed upon the inexperienced operator, therefore, because it is only necessary that Cannabis preparations possess a certain minimum activity and it is not compulsory that they actually be standardized.

Unlike most chemical assays, the assay for Cannabis is such that a preparation which passes the inspection of an inexperienced operator is more active than one passed by the expert because the expert can notice marked signs of incoördination in dogs before the first signs are appreciable to the inexperienced.

Of course, the expert is better qualified to actually standardize these preparations, but, as before stated, a person need not be an expert in order to determine whether or not a particular prepara-

tion of Cannabis conforms to the requirements of the U. S. Pharmacopoeia.

*Aconite*.—The proposed "time limit" of twelve hours is very objectionable as this means twelve hours after the pigs are injected. When you add to this the time of weighing animals, preparing solutions for injections, making injections, etc., the test consumes thirteen hours, which cannot be included in the ordinary working day and makes a rather long week for men employed in laboratories which run these assays almost daily. We would suggest a twenty four hour "time-limit."

Pittenger, by recording the results obtained by using twenty-three and twenty-four hours as a "time limit," proved that the most concordant results are obtained by using twenty-four hours as the "time limit." We do not doubt that a twelve-hour method would be just as accurate as the twenty-four hour method, but it is very objectionable for the reason stated.

We recommend that Gelsemium and Veratrum also be assayed by the Guinea Pig Method.

We cannot too strongly recommend that the biologic assay for Aconite be made compulsory instead of the chemical assay, for while we agree that the chemical assay is a very accurate determination of the alkaloidal content of Aconite, it is not nearly as good an index of the *therapeutic* value of the drug or its preparations, as the pharmacodynamic test, as it has been definitely proven by many workers that the results of the present chemical assay do not parallel the therapeutic activity of the drug.

In other words, it often happens that a preparation of Aconite will run high in the chemical test and low in the physiologic test, due to the fact that a chemical assay does not express the true activity of the drug because it also estimates other alkaloids of lower activity than Aconitine.

This discrepancy between the two tests is easily understood when the nature of Aconitine is considered and it is realized how the acetyl and benzyl groups are split off, thus reducing the physiologic activity of the product without destroying its alkaloidal nature, and allowing it to still be estimated as an alkaloid in the chemical assay process.

The present Pharmacopoeia makes the chemical test compulsory and at the same time recommends that the drug be assayed by the pharmacodynamic method. For the reason stated above, it is

impossible to standardize the product by both methods when the results obtained by one do not parallel those obtained by the other.

We therefore recommend that the pharmacodynamic test be made compulsory in place of the chemical test, or that a double standard, *i. e.*, a chemical standard within a certain range to guard against excessive toxicity and also a minimum biologic standard (a M.L.D.), to guard against inactive or deteriorated preparations be adopted and that preparations which do not conform to both standards be rejected.

*Digitalis-Strophanthus-Squill.*—The principal criticism of the method as given in the Pharmacopoeia is in regard to the technique as recommended for injecting the doses into the frogs.

The U. S. P. states:

"After the frogs have been weighed as described, the doses to be given are calculated according to their weights and are *measured into small conical glasses by means of a finely graduated pipette*. The doses of the preparation which are to be injected should be as uniform in quantity as possible and *should not exceed 0.015 Mil. for each gram of body weight of frog*. . . . When the doses are ready, they may be injected into the anterior lymph sac of the animal. This is done by means of a *glass pipette* which is drawn out to a fine point. The frog is held on its back in one hand and the pipette with the contained drug in the other, the mouth of the frog is opened with the point of the pipette and, carefully avoiding the tongue, the floor of the mouth is punctured and the point of the pipette is then seen to enter the anterior lymph sac of the frog. The contents of the pipette are now forced into the sac either by gravity or by gently blowing, if necessary. In the latter case, care should be taken not to introduce air into the sac."

It is *absolutely impossible* to obtain accurate results if this technique is followed. It will be noted that the average frog should weigh 20 Gm. and that the dose injected should not exceed 0.015 Mil. for each gram or 0.3 Mil. for a 20 Gm. frog. You are directed to measure this 0.3 Mil. by means of a *finely graduated pipette* into a conical glass. This *very small dose* (0.3 Mil.) is then sucked up into another *sharp-pointed pipette* and forced into the lymph sac by blowing.

The error due to the amount of solution left in the conical vessel and the second pipette is indeed great when compared with the very small dose given.

The use of the second pipette and the conical glass vessel is no doubt recommended because it is impossible to force the preparation into the lymph sac by blowing and at the same time accurately measure the dose to the hundredth of a Mil.

The two pipettes and the conical glass vessels should be replaced by an all-glass or Record Tuberculin Syringe, which is graduated in hundredths of a Mil. By the use of one of these syringes the *actual amount of the preparation injected* can be measured to the hundredth of a Mil., whereas by the U. S. P. method we only know the amount of solution placed in the conical vessel and not the amount actually injected.

On page 608, first line, the directions state:

"The dose thus found is then compared, etc."

The text fails to state which dose is the *dose* to be compared. It is not stated anywhere that the smallest or minimum dose necessary to bring about the end reaction is the one to be used in computing the strength of the preparation. In other words, the directions give no definite outline for carrying out the tests, but take it for granted that the operator understands the technique of giving the doses in series, progressively increasing or decreasing until the M.L.D. or M.S.D. is found, etc.

*Suprarenal Gland.*—As stated by Hamilton,<sup>1</sup> "the biologic assay of products of the suprarenal gland is open to criticism in only two particulars, *i. e.*, in the method of measuring and administering the doses and in attempting to check the results as described."

"Using both femoral veins for injecting sample and standard is to obviate the possible mixing of the two solutions if both are injected into the same vein. But it introduces a very much greater source of error. The amount injected can much more easily be measured by use of a pipette than in a syringe, and the dose after being injected can be easily and completely washed into the blood stream by a follow-up injection of 2 Mils. of physiologic salt solution. When this procedure is followed, no mixing of two injections is possible."

Another very good method is to *expose the saphenous vein at its junction with the femoral*. When giving injections, the needle of an all-glass syringe is inserted far enough through the saphenous vein to allow the point to project directly into the blood stream in the femoral vein. After injecting the preparation, the needle can be

<sup>1</sup> Hamilton: "Biological Standardization," *THIS JOURNAL*, February, 1917.



withdrawn and the saphenous vein clamped with a bulldog clamp. The preparation thus injected is entirely carried into the circulation by means of the main current of blood in the femoral vein.

The "checking of an assay by making injections of the sample and of the standard into opposite sides from the first used is no check except in so far as it checks conditions on the two sides of the dog. This feature can better be eliminated by using only one side. Further, by the official method, if it is impossible to complete the test and the check on a dog, no option is left, but to repeat both test and check on another dog. It is occasionally necessary to check an assay on a second dog when conditions during the first test were unfavorable to accuracy but no advantage results from a retest on the same dog."

*Pituitary Extracts.*—We strongly recommend that the Isolated Uterus method be retained as the official method for testing Liquor Hypophysis.

Several papers have been written recommending the blood pressure method, but our experience has been that the isolated uterus method is the best so far proposed, as differences of activity which are only just appreciable by the blood-pressure method, under the best conditions, are at once obvious in the test on the uterus without any special care in controlling the regularity of the response.

We are of the opinion, however, that more concordant results can be obtained by employing the *whole* one horn of the uterus of a 350 to 425 Gm. pig as suggested by Pittenger,<sup>1</sup> instead of only a *segment* of the one horn of the uterus of a 250 Gm. guinea pig; also by controlling the contractions of the uterus by means of an escapement wheel and bucket for holding shot instead of the small heart lever recommended. When the whole horn is used, the heart lever is not heavy enough to allow sufficient weight to be added to control the contractions of the muscle.

The assay for Liquor Hypophysis requires more experience on the part of the operator than any other biologic test in the Pharmacopoeia, and, although compulsory for a U. S. P. product, it is not included in the chapter on "Biologic Assays."

Under "Liquor Hypophysis," however, we find that the product must be tested "as directed by the United States Hygienic Labora-

<sup>1</sup> Pittenger: "An Improved Apparatus for Testing Drugs upon the Isolated Uterus," *Jour. A. Ph. A.*, June, 1918.

tory." We would recommend that the complete details of this test should be included in the U. S. P.

The principal criticism of the U. S. P. method for testing Liquor Hypophysis, however, is not with the method itself but with the standard adopted.

Before readopting a complex substance like Beta-aminazolyethylamine Hydrochloride as a standard for adjusting the strengths of commercial preparations, a thorough study of the following points should be made:

1. Degree of uniformity in the physiologic action of different available samples of the proposed standard substance.
2. Rate of deterioration of solutions of this substance.
3. Effect of sterilization on solutions of this substance.
4. Rate of deterioration of the substance itself.
5. Effect of repeated doses on uterus.
6. The toxicity of the substance as compared with Pituitary Extract.
7. The relative toxicity of a Pituitary Extract of the strength proposed by the U. S. P. IX and that of the commercial extracts as supplied by the leading pharmaceutical manufacturing houses.

The standard adopted by the U. S. P. IX is very low, it having been shown by comparison that the commercial extracts prepared by the leading pharmaceutical houses, which have had preparations on the market for several years and with which the physicians have become accustomed as to dosage, etc., are from three to five times as active as an extract of the U. S. Pharmacopoeia standard strength. This is unfortunate, as there is no reason why a weaker preparation than the one to which physicians have become accustomed should be placed on the market.

It is hoped, therefore, that if this substance is retained as the standard test substance, definite requirements as to its purity and uniformity of activity can be drawn up, and that an accurate co-ordination of the required U. S. P. strength and of the common pharmaceutical practice may be secured.

#### DRUG ASSAY

The methods given in the U. S. P. for drug assays are generally quite satisfactory and there are but a few alterations necessary. The chapter on proximate assays in Part Two is particularly to be commended, as it is clear, complete and informative. The errors

found are merely those of phraseology; for instance, in the first paragraph on page 593 it is stated that alkaloids "are more or less soluble in alcohol, chloroform, ether, amyl alcohol, benzene, petroleum benzin, or mixtures of several of these." The latter phrase is somewhat misleading, as it conveys the impression that the alkaloids are not soluble in a mixture of two of the solvents but only in a mixture of more than two, or, in other words, of several. In our opinion, the latter part of this sentence should be changed to read as follows: "More or less soluble in alcohol, benzene, petroleum benzin, or a mixture of two or more of these." The same sort of error occurs in paragraphs three and four, page 594. In paragraph three it is stated that a mixture of *more* than one volume of chloroform to one volume of ether will separate in the bottom of the separator. As a mixture of equal volumes of chloroform and ether is also heavier than water, the sentence should read as follows: "A mixture of one volume or more of chloroform to one volume of ether will settle in the bottom of the separator." The correction of paragraph four is of the same order, as the phrase should read: "Two volumes or more of ether to one volume of chloroform."

*Indicator.*—It is recommended that *methyl red* be specifically directed for use in the various assay processes instead of cochineal. Methyl red gives clear end-points in all cases, whereas the end-point with cochineal, when assaying aconite, ipecac, nux vomica, or opium, is rather obscure and difficult to determine. Cochineal could be permitted for alternate use as methyl red now is.

*Detection of Alkaloid.*—On page 594, in paragraphs five and six, under the instructions for determining the presence or absence of alkaloid during the various stages of the assay, it is stated that the solution tested should show not more than a very faint cloudiness on the addition of a drop of mercuric-potassium iodide T. S., or in the case of caffeine or colchicine on the addition of a drop of iodine T. S. Experience has shown that it is necessary to "shake out" until a negative test has been obtained, particularly in the case of extracts, such as powdered and solid extracts of belladonna leaves, which require more than the usual number of shake-outs. Ordinarily, and particularly in the case of crude drugs, three or four shake outs are sufficient to extract all of the alkaloids, but in the case of the belladonna and other extracts many more shake outs are

usually needed to extract all of the alkaloid. A faint cloudiness may be obtained after each of a number of extractions, due probably to the difficult solubility of the alkaloid. In the aggregate, the alkaloid extracted by each of these shake-outs represents a substantial quantity, particularly if the lot being assayed is a large one. In view of these facts, we recommend that the words, "not more than a very faint," as found on lines twenty-six and thirty-nine (page 594) be omitted and the word "no" substituted so that the phrase shall read: "Shows no cloudiness on the addition of."

*Determination of Alcohol-Soluble Constituents.*—A standard method for the determination of the alcohol-soluble constituents of asafoetida, benzoin, gambir, gamboge, kino, and myrrh is needed. A continuous extraction method is recommended because of its ease of operation and the saving of time and solvent. As some of the constituents dissolve rather slowly a test should be included to determine if the extraction is complete.

*Menstrum for Assay of Crude Drugs and Extracts.*—Considerable trouble has been experienced with the menstrum composed of ether, two parts, and chloroform, one part, which is directed to be used as the macerating medium, in various assay processes, as given under belladonna root. An ether chloroform mixture in these proportions is not satisfactory on account of a strong tendency to form emulsions. Complete contact of all portions of the two layers of liquid is quite difficult and much more time is required on account of the necessity of using much care during the agitation. The disintegration of emulsions is also time consuming, so that this factor, together with the other factors, previously stated, renders it necessary to change the proportions of ether and chloroform used as menstrum or solvent. The menstrum of three parts of ether and one of chloroform, as used in the U. S. P. VIII, is much more satisfactory as it permits a more vigorous agitation and a complete contact of the two layers. A menstrum composed of these proportions of ether and chloroform is much less likely to form emulsions and gives a cleaner separation of the two layers. We therefore earnestly recommend the re-adoption of the menstrum of ether, three parts, and chloroform, one part, as formerly used in the U. S. P. VIII.

*Assay of Fluid and Solid Extracts and Tinctures.*—The assay of solid extracts of belladonna, hyoscyamus, and stramonium could be simplified and shortened if a maceration method, such as that used for powdered extracts were adopted. The present method of dis-

solving the extract in dilute alcohol and transferring directly to a separator, gives considerable trouble, on account of the formation of emulsions, which is partly due to the unavoidable presence of undissolved matter. Instead of a direct shake-out, we recommend that the extract be dissolved in a suitable solvent, spread over oak sawdust, evaporated at a low temperature, transferring to a flask and treating in the manner described for powdered extract of belladonna. Similar methods could be used for fluid extracts of belladonna, guarana, hydrastis, hyoscyamus, and nux vomica, and also tinctures of belladonna, hydrastis, hyoscyamus, nux vomica, and stramonium. At present the maceration method is used for fluid extracts of aconite, cinchona, ipecac and pilocarpus and tincture of aconite, cinchona, and physostigma. The application of the maceration method would decidedly lessen the danger of emulsification and requires a fewer number of shake-outs to extract the alkaloid.

*Physostigma*.—The U. S. P. method for the assay of this drug and its preparations has been found to give erroneous results. Low results have been consistently obtained and are probably caused by the heat used in the assay, and to some extent by incomplete extraction. As a substitute method we offer for consideration the method devised by Mr. George E. Éwe, which was published in the December, 1919 number of the *Journal of the American Pharmaceutical Association*. This method eliminates most of the heating and has given satisfactory results in the H. K. Mulford laboratories.

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## CONCENTRATED MILK PRODUCTS.\*

By J. W. ENGLAND,

PHILADELPHIA, PA.

CONDENSED MILK.

Condensed milk is an evaporated milk representing about two and a half times its volume of fresh milk and containing about 40 per cent. by weight of cane sugar. It is of thick syrupy consistency and very sweet taste, and is marketed in cans. Commercially, it is made by dissolving cane sugar in fresh milk by a warming pan, after which it is drawn into the vacuum pan where it is condensed

\* Read before the annual meeting of the Pennsylvania Pharmaceutical Association, held June, 1920.

at a temperature of 120° to 130° F. until the volume of liquid is 40 per cent. or less of the original volume; if the milk be overheated, the albumin will be coagulated and the sugar caramelized. After condensation, the milk is drawn off into cooling cans and constantly stirred in a sanitary room and atmosphere for two or three hours until a temperature of 70° F. is reached, when it is quickly canned and sealed.

Some of the more modern canners of milk, sterilize the cans with dry heat before filling them, but the cans are cooled *in vacuo* before being filled, otherwise the milk congeals. If the milk condensed be acid,\*a certain amount of invert sugar (dextrose and levulose) is formed. Some manufacturers use invert sugar in place of cane sugar (U. S. D. 20 Edt., 1498), because invert sugar has a less sweet taste than cane sugar and is less liable to cause sugar of milk to crystallize in the can.

According to Food Inspection Decision No. 170 (U. S. Department of Agriculture, March 31, 1917), condensed milk must be the product of the evaporation of whole, fresh, clean cow's milk and must contain at least 8 per cent. milk fat and not less than 28 per cent. total milk solids.

Condensed milk is not sterile and may contain pathogenic organisms; it is preserved against decomposition by its high percentage of sugar, which also prevents freezing during transportation. So long as the can is unopened, condensed milk will keep under favorable conditions for a year or two, but after several months it becomes darker in color and thicker; when the can is opened, if kept in a cool and sanitary place, it will keep for several days.

Condensed milk was the first form of canned milk put on the market. "The early French inventors along this line, dating back over a hundred years, are said to have been called forth by Napoleon's efforts to obtain a milk that could be transported for the use of his armies. It is interesting to note that canning milk first became a successful enterprise because of the urgency in this country of feeding the soldiers of the North in the Civil War." ("Condensed Milk and Milk Powder:" Otto F. Hunziker. Published by the author, Lafayette, Ind., 1914.)

During the recent World War, the demand for condensed milk was enormous. Mr. Charles E. Hires, of Philadelphia, one of the leading manufacturers of condensed milk in the country, writes me as follows:

"Following the thought expressed by you yesterday relative to the production of condensed milk in the United States, it gives me pleasure to enclose herewith the data of same:

I do not have an accurate record of the amounts produced in 1914 and 1915, but the amounts exported were as follows:

	Pounds.
1914	22,850,904
1915	75,689,584

The amounts manufactured and exported were as follows:

	Pounds.	Pounds.	Percentage Exported.
1916	992,364,000	219,686,127	22
1917	1,333,787,000	428,575,213	32
1918	1,675,934,000	551,139,754	33
1919	2,030,958,000	852,865,414	42

The number of cases of condensed and evaporated milks manufactured were as follows:

1916	Condensed	5,931,000
	Evaporated	14,474,000
1917	Condensed	7,482,000
	Evaporated	19,618,000
1918	Condensed	10,188,000
	Evaporated	22,998,000
1919	Condensed	13,441,000
	Evaporated	25,720,000

I believe these figures to be reliable. The data was compiled by The National Cannery Association of Washington, D. C."

"Milk," an exceedingly informative pamphlet issued by the U. S. Department of Labor, Childrens' Bureau, No. 35, 1918; written by Dr. Dorothy Reed Mendenhall, and from which considerable data in this article have been taken, gives the following average percentage composition of condensed milk:

AVERAGE COMPOSITION OF CONDENSED MILK (HUNZIKER).

Fat.....	9.0
Protein.....	8.5
Milk sugar.....	13.3
Cane sugar.....	40.9
Ash.....	1.8
Water.....	26.5

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100.0

One of the best known brands of condensed milk, can marked "net weight 15 ounces," has upon its label the following statement: "By adding 1 part of water to 1 part of the contents of this can, a resulting milk product will be obtained which will not be below the legal standard for whole milk." Presumably, *parts by volume* are meant—not parts by weight. On examining this condensed milk, I found it had a specific gravity of about 1.26 and one tablespoonful (rounded) weighed about 350 grains. (The tablespoon is the usual form of measurement for the smaller dilutions.) Therefore, one tablespoonful of the condensed milk mixed with one tablespoonful of water represents, practically, 60 per cent. by weight of condensed milk; with 6 tablespoonfuls of water represents 20 per cent. by weight; with 12 tablespoonfuls of water represents 11 per cent. by weight; with 18 tablespoonfuls of water represents 8 per cent. by weight. With these factors the percentages of the food elements in the different dilutions when measured by the tablespoon can be readily ascertained.

But the tablespoon "heaps" when filled with condensed milk, measuring more than 240 minims (as with water). Hence, one fluid ounce of condensed milk (S. G. 1.26) weighs about 575 grains and mixed with an equal volume of water represents, practically, 56 per cent. by weight of condensed milk, with 6 fluid ounces of water, represents 17 per cent. by weight, with 12 fluid ounces of water represents 9.5 per cent. by weight, and with 18 fluid ounces of water represents 6.5 per cent. by weight.

In making condensed milk dilutions for infant feeding, the graduated measure should be used instead of the tablespoon; it is much more accurate.

Condensed milk is often useful for feeding infants, but it has its limitations. It "is advisable for temporary use during attacks of indigestion, for infants with feeble digestion, especially in summer, for very young infants during the first two or three months, or among the very poor when the cow's milk which is available is still more objectionable" (Holt), and also for undernourished infants where the use of a rapidly assimilable body fuel like sugar is indicated. In traveling, it is most convenient as well as the safest food to use. It is usually diluted six times or more with water, according to age. But condensed-milk-dilutions are illy-balanced, physiologically, containing low percentages of fat and protein and a high content of sugar, and hence, even if prepared under the best possi-



ble conditions, "should not be used as a permanent food when good fresh cow's milk can be obtained" (Holt).

The composition of human milk averages fat 3.5 per cent., protein 1.5 per cent., and sugar 7 per cent.; cow's milk averages fat 4 per cent., protein 3.5 per cent., and sugar 4.50 per cent. The U. S. (Federal) minimum standard for cow's milk is fat 3.5 per cent., non-fatty solids 8.5 per cent. (U. S. D. 20th Edit., 1918, 1498).

#### EVAPORATED MILKS.

Evaporated milk, formerly mis-named evaporated cream, is an evaporated milk representing from two to two and a half times its volume of fresh milk and containing no cane sugar. It is an unsweetened condensed milk. It has the consistency of thin cream and is much less sweet than condensed milk. It is sold in cans and in many large cities is delivered fresh daily in bulk.

Commercially, it is made by evaporating fresh milk *in vacuo* until the volume of liquid is from 40 to 50 per cent. of the original volume, placing it in cans and then sterilizing the contents by subjecting the cans to steam under pressure. The temperature must be "high enough and maintained long enough to insure absolutely sterility to the product and to give the milk sufficient body to prevent the separation of the butter fat in subsequent transportation and storage." ("Milk," U. S. Department of Labor, Bulletin Publication No. 35, 1918.)

The Federal regulations require that evaporated milk must be made from whole, fresh, clean cow's milk and must contain at least 7.8 per cent. fat and not less than 25.5 per cent. total milk solids (Food Inspection Decision No. 158, U. S. Department of Agriculture, April 2, 1915). It will be noted that the standard required for milk solids in evaporated milk is nearly the same as that for condensed milk.

Evaporated milk is, or should be, absolutely sterile and will keep almost indefinitely so long as the can is unopened; once opened, however, it rapidly decomposes (but does not sour first, like condensed milk, it putrefies); it should be kept well iced and used in a day or two.

*Chemical Age* (June, 1920, 188) states that: "As a matter of more than passing interest it should be noted that evaporated milk, part or full skimmed, modified with foreign fat or vegetable oils, has been used in increasing quantities as a substitute for true

evaporated milk for home consumption. While but 12,000 pounds were tinned in 1916, more than 62,000,000 pounds of the case goods were manufactured in 1919, as shown by the following table. In 1916, the production of the substitute compared with the production of true evaporated milk, case goods, was negligible, while the production had increased to over 5 per cent. by the close of 1919:

PRODUCTION (IN POUNDS) OF EVAPORATED MILK (PART OR FULL SKIMMED)  
MODIFIED WITH FOREIGN FAT IN THE UNITED STATES, 1916-1919.

Year.	Case.	Bulk.	Total.	Increase Over Previous Year. Per cent.
1916	12,000	14,134,712	14,146,712	...
1917	18,504	17,487,064	17,505,568	24
1918	41,033,855	7,591,182	48,625,037	178
1919	62,262,221	2,748,120	65,010,341	34

"Milk" (1918, 20) gives the following average percentage composition of evaporated milk:

AVERAGE COMPOSITION OF EVAPORATED MILK (HUNZIKER).

Fat.....	8.3
Protein.....	7.5
Milk sugar.....	9.7
Ash.....	1.5
Water.....	73.0
	<hr/>
	100.0

Dr. D. R. Mendenhall states that "from the feeding experiments recently conducted on animals it does not seem probable that either of the vitamins so far determined is injured by the high temperature. By diluting with equal parts of sterile water, evaporated milk can be reconstituted, approximately, as ordinary milk; also, it can be of great use in the general nutrition of the household and it certainly has a more tenable place in the feeding of infants and young children, when fresh milk cannot be obtained, than condensed milk. We must recognize the facts that it will freeze and is, therefore, not suitable for transportation in cold weather; that it must be carefully handled after opening the can, if it is to remain a sterile food and one fit to give an infant; and that even though condensed to one-half to two-fifths of its original bulk, it is still bulky to transport. Also, all condensed milk is relatively high in price as compared with grade A, raw milk \* \* \* \* . All these reasons make evaporated milk far from the ideal substitute for fresh milk."

Dr. L. Emmett Holt ("Diseases of Infancy and Children," 1916, 159) states that: "Evaporated milk requires the same modification (for infant feeding) as ordinary cow's milk. For routine use, it should be diluted with from eight to twelve parts of water and sugar added. \* \* \* \* It is a sterile cooked milk. Some children thrive upon it who cannot so well digest either raw milk of the same percentage composition or even freshly pasteurized milk. It should not be continued as the sole food when good fresh cow's milk can be obtained."

One of the best known brands of evaporated milk, can marked "net weight 1 pound," has upon its label the following statement: "By adding one part of water to one part of the contents of this can, a resulting milk product will be obtained which will not be below the legal standard for whole milk. Presumably, *parts by volume* are meant, not parts by weight.

On examining this evaporated milk, I found that it had a specific gravity of about 1.07, and one tablespoonful weighed about 256 grains. Therefore, one tablespoonful of the evaporated milk mixed with one tablespoonful of water represents, practically, 53 per cent. by weight of evaporated milk; with 6 tablespoonfuls of water represents 15.75 per cent. by weight; with 12 tablespoonfuls of water represents 8.5 per cent. by weight; with 18 tablespoonfuls of water represents 6 per cent. by weight.

With these factors, the actual percentages of the food elements in the different dilutions measured by the tablespoonful can be readily ascertained.

Evaporated milk does not "heap" on the tablespoon like condensed milk and, therefore, does not bulk so large. One fluid ounce of evaporated milk (sp. gr. 1.07) weighs about 488 grains and mixed with an equal volume of water represents, practically, 51.7 per cent. by weight of evaporated milk, with 6 fluid ounces of water represents 15 per cent. by weight, with 12 fluid ounces of water represents 8 per cent. by weight, with 18 fluid ounces of water represents 5.5 per cent. by weight.

In making evaporated milk dilutions for infant feeding, the graduated measure should be used instead of the tablespoon; it is more accurate.

#### DRIED MILKS.

Dried milk is milk deprived of its water, or the milk solids, and represents about eight times its weight of milk. It is a yellow.

fluffy powder that is readily miscible with water, forming a milk-like liquid having a cooked milk taste. Dried half-cream milk is similar but is made of milk from which one-half the cream has been removed, and is a light yellow, fluffy powder. Dried skim milk is made from skim milk and is a yellowish white, granular powder.

Commercially, according to "Milk" (1918, 21), milk powder is made by one of the following processes: (1) By feeding the milk in a thin stream over two steam heated cylinders or drums, about one-eighth inch apart, revolving in opposite directions. The milk exposed to the heat of the cylinders dries as a thin film and comes off the revolving cylinder as a sheet, which is easily crushed into a fine powder. The cylinders which are some 60 inches long and 24 inches in diameter are charged with steam under two or three atmospheres of pressure, causing the heating surfaces to have a temperature of about 250° to 280° F. This process, known as the Just patent in the United States and as the Just-Hatmaker patent in England, is said to have been the invention of J. R. Hatmaker of London; (2) by pasteurizing milk and then condensing in the vacuum pan, at a low temperature (130° F.), to about one-fourth its bulk, after which the condensed product is forced under high pressure through minute openings in a metal disk into a hot air chamber. The atomized liquid surrounded by a current of hot air instantly dries and falls to the bottom of the chamber as a snowy powder, the moisture rising as a cloud of steam. The mixture of the liquid and air in the evaporating chamber is stated to be about 180° F. The method was developed in France and is called there and in England the Bevenot de Neveu process. In this country it is known as the Merrell-Gere process; (3) by condensing milk to approximate dryness in a vacuum pan equipped with a mechanical stirrer.

The Federal regulations (Food Inspection Decision No. 170), U. S. Department of Agriculture, March 31, 1917), require that dried milk must contain "not less than 26 per cent. milk fat and not more than 5 per cent. of moisture." There are no Federal standards, apparently, for dried half-cream milk and dried skim milk, except that the latter "shall not contain more than 5 per cent. of moisture."

Dried milk and dried half cream milk are sterile and in sealed cans keep almost indefinitely. Exposed to air, warmth and moisture, however, they slowly become rancid; dried skim milk, however,

with its low content of fat, remains unchanged longer. The dried milks should be stored in a cool and dry place.

Eric Pritchard (*Medical Press and Circular*, Vol. 97: 192-195 (Feb. 25) 1914) gives the following as the average percentage composition of the dried milks:

	Casein.	Albumin.	Sugar.	Fat.	Calories per Oz.
1. Dried milk.....	24.50	1.94	38.92	28.00	146
2. Dried half-cream milk....	30.58	2.42	39.70	15.10	119
3. Dried skim milk.....	31.40	2.49	55.00	1.00	104

The dried milks are now made upon a very large scale and find different uses according to kind. They are used in manufacturing confectionery, such as milk chocolate, baked food products and ice cream, etc., and should find a ready application for soda fountains and in the household. Their utility in traveling is obvious. They possess many advantages—sterility, stability, convenience and cheapness.

Dried half-cream milk is used for infant feeding, more especially in France and England, being similar in such application to evaporated milk. Two ounces by weight mixed with sufficient hot (not boiling) water to make 1 pint, gives a liquid that, except for deficiency in fat, approximates the composition of cow's milk, as follows: Fat 1.5 to 2 per cent.; protein 4 per cent., sugar 5 per cent. Dried whole milk mixtures are used, also, for infant feeding, especially for infants over six months of age.

Dried skim milk is used in making bread, rolls, muffins, cakes, custards, creamed soups, sauces and vegetables, cocoa and chocolate; if richer products be wished, the dried milk or dried half-cream milk is employed.

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## THE MEDICAL DIVISION OF THE NATIONAL MUSEUM.

BY CHARLES G. MERRELL,

CINCINNATI, O.

Those of you who have kept in touch with the proceedings of the American Pharmaceutical Association will recall that some years ago an effort was made to bring about the establishment of a national pharmaceutical museum at Washington, where material bearing upon pharmaceutical history might be collected and deposited for future reference.

The Historical Section of the American Pharmaceutical Association has, for years, busied itself with the collection of historical material of various kinds, and it was largely with a view to providing a permanent home for such material that the movement for a national depository for matters of historical interest from a pharmaceutical standpoint was carried on.

This end has at last been achieved through the enlargement of the field of the Smithsonian Institution, which now, under the name of the National Museum, has established a very interesting medical division, which includes much matter of interest to pharmacists.

This medical division is located on the south side of the gallery in the East Hall of the Arts and Industries Building of the Museum

The subjects illustrated are grouped under four heads, namely:

- (1) History of Medicine.
- (2) *Materia Medica*.
- (3) Pharmacy.
- (4) Sanitation and Public Hygiene.

Three alcoves are devoted to the history of medicine, starting from the beginning of medicine in India, Egypt, Greece, Rome, China, and among the Hebrews.

Two alcoves are devoted to the history of medicine in America, which is illustrated by biographical sketches, portraits, etc.

Three alcoves are devoted to *materia medica*, and two to pharmacy, including both modern and historical pharmacy. It was through the efforts of Mr. F. L. Lewton that the section of pharmacy was established.

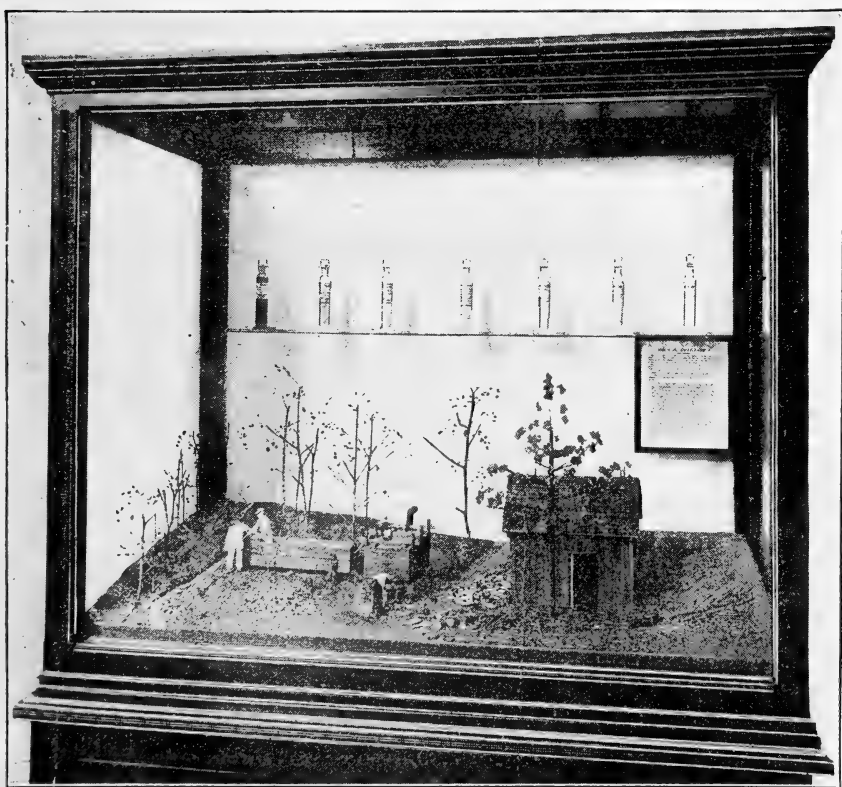
Several of the leading manufacturers of the United States have contributed material illustrating the lines in which they are interested and the products they prepare.

Many of the members attending the meeting of the American Pharmaceutical Association and of the delegates attending the Tenth Decennial Convention for the revision of the United States Pharmacopoeia at Washington in May took the occasion to visit the National Museum and see the display of articles of medical interest which has been organized there in the Medical Division under the supervision of Mr. F. L. Lewton, curator, and of Mr. C. Whitebread, the assistant curator of that division.

Through the courtesy of Mr. Whitebread I am able to present a photograph of one of these displays which will give an idea of the

pains which the museum authorities have taken in the preparation of the exhibit.

The still shown in the accompanying illustration is used for the distillation of the oil from the bark of the *Betula Lenta*, the black or sweet birch which abounds in the mountains of the Carolinas, eastern Tennessee, Kentucky, and some sections of Connecticut and Pennsylvania. In Connecticut the oil is obtained from the twigs of the small birch bushes, the supply of trees having been exhausted.



Distilling Birch Oil in the Carolina Mountains.

From a model shown in the Medical Division of the National Museum at Washington.

The illustration shows a model of a North Carolina still in operation which is exhibited in the Division of Medicine of the National Museum at Washington. The exhibit was prepared under the supervision of Mr. C. Whitebread.

The still used in the Carolinas is about 8 or 10 feet long and about 4 or 5 feet high and about the same width. The still is made of wood, except the bottom, which consists of sheet iron. Between 8 and 9 inches from the bottom is a false bottom of wire mesh or perforated sheet iron.

In Connecticut, however, the industry is on a more permanent basis. The stills are larger and more effective than that shown in the illustration, and each distillery has a warehouse in which it stores the twigs and brush which are used for distillation, these plants being quite extensive and representing considerable investment.

In Carolina the distiller buys the bark privilege from some lumber company, and under this privilege cuts down the birch trees, paying a stipulated sum for each tree used. These trees run up to as much as 10 or 12 inches in diameter.

When the tree is cut down the buyer removes the bark by beating the trunk and the larger branches with a maul, and carries the bark thus obtained to the still in baskets.

The bark is laid on the false bottom of the still, about 40 bushels constituting a charge, and the cover is fastened on with wedges as shown in the illustration.

The outlet of the still is an ordinary gas pipe, generally from  $\frac{1}{2}$  to 1 inch in diameter and about 10 feet long. This is encased in a long box or trough through which a stream of water flows, condensing the mixture of steam and oil which comes off. The bark is first steamed for about 12 hours, as the oil does not exist in the bark as such, but as a glucoside which is hydrolyzed by the steaming and thus yields oil. The heat is then raised sufficiently to insure distillation, which goes on generally for about another 12 or 14 hours, making 24 to 28 hours to run a charge.

One ton of green bark will usually yield about three pounds of oil. The bark which has been distilled serves as fuel for the next charge.

The distillate, consisting of a mixture of oil of birch and water, is collected in a funnel placed in an ordinary Mason jar placed on a hollowed receptacle. The oil of birch settles to the bottom and the milky mixture of oil and water overflows the jar and passes down through the receptacle beneath the jar into a small pipe which leads into the still below the water level.

The apparatus is, therefore, in the nature of a continuous reflux still, though in a very crude form.



In the bottles above the model are shown samples of the oil and its derivatives, natural salicylic acid in large and in small crystals, and the sodium, lithium, strontium and magnesium salts of that acid.

This particular exhibit interested me for the reason that such great difficulty has been experienced in obtaining pure birch oil that we have found it necessary to purchase and operate our own stills. I was also interested from the therapeutic point of view, for I am firmly convinced that better therapeutic results are obtained from the natural acid and its salts than are obtained from the use of the synthetic product, and my belief is shared by a large number of practicing physicians. I am in receipt of a note from Mr. Whitebread on the subject, who writes: "The Museum desires to have the state pharmaceutical associations advised of its efforts to collect articles bearing on the history of pharmacy in the United States and appreciates very much your coöperation in presenting the matter to the Ohio Pharmaceutical Association at this time. The task of collecting proper material relating to pharmacy is an immense one when placed in the hands of one or two men, but if all pharmaceutical associations will bear in mind our efforts and do their bit by calling to the attention of the Museum information where historical material can be obtained the task will be an easy one and it will not be long before we shall have a national collection which will be worthy of the subject which it represents."

In order to make a beginning in this direction I would suggest that a committee on National Museum Exhibit be appointed by each of the State pharmaceutical associations, whose object it shall be to coöperate with the Museum authorities in collecting suitable material to add to the pharmaceutical exhibit.

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### "I WILL"—THE CREED OF A SUCCESSFUL DRUGGIST.

BY FRANK H. WILLIAMS,

FORT WAYNE, INDIANA.

I will make my window displays attractive, timely and interesting and I will vary them frequently because I realize that window displays advertise my goods to folks at the point where the goods are on sale and are, therefore, just about as effective and inexpensive advertising as I can possibly engage in.

I will sell customers the sort of articles they want to buy instead of trying to make them purchase the things I want to sell, because I realize that by doing this I will be making friends instead of dissatisfied purchasers.

I will keep my show rooms neat and pleasing because I realize that people prefer trading in attractive places instead of doing business in poorly lighted and dowdy-looking rooms.

I will do a certain amount of newspaper advertising, not more than my business can afford, and I will try to make this advertising snappy and different because I realize that there is so much advertising of the ordinary kind that it takes a different slant from the usual in newspaper publicity to make people sit up and take notice.

I will watch my charge accounts carefully, send bills regularly, and make a real effort to collect overdue accounts because I realize that the loss on one charge account which isn't paid, frequently eats up the profits on a number of cash sales.

I will read my trade paper carefully and note the various points it emphasizes because I realize that my trade papers are published for the purpose of helping me make more money out of my business and that from them I can secure many valuable pointers.

I will take my proper place in civic and commercial affairs because by so doing I will enhance my prestige in the community and because I realize that the greater my prestige is the more business I will do.

I will see to it that my employees extend to customers a constant courtesy and service because I realize that courtesy and service are two of the most important factors in building up and keeping a good trade.

I will be fair and square in my dealings with my customers and with the houses from which I purchase goods because I realize that the Golden Rule is still the best rule for the successful conduct of modern business.

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### THE ETHICS OF PRESCRIBING.\*

BY JAMES BURNET, M.A., M.D., M.R.C.P.,

EDINBURGH, SCOTLAND.

Probably few medical men have reflected that there are certain ethical matters relating to a prescription. In fact a prescription may do a great deal of good, but at the same time it may work much harm. We shall endeavor in this short article to point out certain

\* From *The Prescriber*, July, 1920.

facts, which, if borne in mind, will save endless trouble and render the prescription a much more valuable thing than it otherwise would be.

In the first place, the prescription should contain no ingredient or ingredients whose action is not known to the profession. Many American and foreign concoctions are largely advertised, but no one can really say why they are beneficial, if indeed they ever are. Some medical men get into the habit of ordering a ready-made formula, which perhaps consists of a dozen different ingredients, just because it has been brought to their notice by the manufacturers. Such prescriptions are ethically bad, and should not be encouraged. One often hears the remark that patients like out-of-the-way things, and that ladies like to be told to get a bottle of compound elixir of "ovario-thymo-thyroid," and to take a teaspoonful after every meal. Probably if they were given a prescription for rhubarb and soda they would think the physician a very ordinary man. All this, however, savours of quackery, and ought not to receive the sanction of members of a scientific profession. We once heard of a very good country doctor who gave a patient a prescription containing iron and arsenic in pill form. She happened shortly afterwards to be on a visit to some friends, and she was advised to consult a "famous specialist." He told the lady to get a box of iron and arsenic capsules at a certain shop in that particular city. For this word-of-mouth advice she paid three guineas, and, of course, valued it accordingly. She continued to have these capsules sent to her in the country, and altogether ignored the pills containing exactly the same ingredients. Certainly the public are very gullible where drugs are concerned, but it is our bounden duty not to pander to their gullibility by giving prescriptions likely to appeal to the imagination in this way.

The fact that very few medical men know how to write prescriptions is probably accountable for another breach of ethical prescribing. We refer to the common custom of simply telling the patient what to get. This is a most reprehensible practice, and does the doctor a great deal of harm, besides giving the patient a foolish sense of medical knowledge. "Take a pinch of chlorate of potash and dissolve it in a teacupful of water." "Get half a dozen 15-grain bromide of potash powders, and take one at bedtime." "I'll repeat your arsenic mixture." "I'm going to give you a prescription for strychnine and hydrochloric acid." "Go to the chemist and get

an ounce of solution of arsenic and take five drops in water thrice a day." "Your child needs belladonna, and I'll give you a prescription for the tincture." "I think veronal would set you to sleep; you had better get a bottle of tablets and take one or two at bedtime." "Have you tried the syrup of codeine? Get some out of the chemists, and take a teaspoonful now and again." "Get a drachm of boric acid crystals and shake them up in a pint of water." These orders are culled from notes in our possession which might be entitled "The Big Blunders Some Doctors Make." It is most unethical to order drugs in this way. Moreover, it is often extremely dangerous. It may happen that the chemist is too careful to supply dangerous drugs when ordered in such a slipshod fashion, but too often he is tempted to supply what is asked lest he lose his customer's patronage. It is a golden rule, which should be strictly adhered to in every case, never to order any drug save by means of a properly worded prescription.

In prescribing dangerous drugs such as morphine, arsenic, veronal, and all hypnotics, it is very essential that the words "not to be repeated" should be written across the prescription in order to prevent the patient from having it dispensed again and again on his own initiative. We have known of a case in which a patient had a prescription for digitalis which he used himself and handed to some of his friends who were supposed to be similarly affected. In writing prescriptions containing cocaine special care has to be exercised. We find that there are still one or two medical men who are ignorant of the legal requirements in such cases. The prescription must contain the full name and address of the person for whom the drug is ordered, must be dated, and signed by the full name, qualifications, and address of the physician. It must also bear the words "not to be repeated." Failure to comply with these requirements entails a penalty, which has been inflicted already on more than one unsuspecting practitioner.

There is such a thing as a "slovenly prescription." This is a term which we find very applicable to the carelessly written and often very illegible prescriptions of doctors with large practices. This remark applies specially to those engaged in health insurance work. The use of "drapery bill" prescription forms ordered by the Commissioners has intensified this evil. We have seen prescriptions of the type referred to, and we think that they reflect little credit on the doctors who wrote them. Of course, we cannot

expect good work if it is not paid for, and until doctors receive some encouragement from the powers that be they will continue to give but scant heed to the writing of their health insurance prescriptions. A slovenly prescription is never ethical. It cannot, on the face of it, conform to the fundamentals of a good prescription.

To be strictly ethical a prescription should fulfil all the following essentials:

(1) It should be carefully written on a sheet of notepaper, not on a scrap of anything that comes handy.

(2) It should preferably be written in ink.

(3) It should contain the name (and probably also the address) of the patient for whom it is intended, and should always be dated.

(4) It should contain carefully worded directions for its use.

(5) It should be initialed (or preferably signed) by the writer.

(6) When it contains dangerous ingredients the words "not to be repeated" ought to be incorporated.

(7) It should contain no incompatibility or any proprietary remedy whose action is unknown to the prescriber.

These fundamentals aim high, perhaps; but after all is it too much to ask that a scientific man should exercise very great care in giving what is, perhaps, to the patient the most essential part of his services? The patient is unusually observant in such matters, and if he notices any carelessness on the part of the doctor in writing the prescription his confidence is apt to be somewhat shaken.

Students too often qualify without having had their attention drawn to these matters. The modern tendency is to discount prescription-writing altogether, and to store the mind with pharmacological actions, most of which have not been put to any real clinical test, and consequently are of comparatively little value from the point of view of the actual practice of medicine. A lecture or two on the ethics of prescribing would be of infinitely more practical value than numerous exhortations on the effects of digitalis and other drugs on the frog! We have not to deal with frogs but with human beings, and pharmacology becomes valueless to the student unless it is taught from the clinical standpoint. The doctor who can write a good ethical prescription is a safer man than one who has merely a knowledge of drugs as they have been used in the research laboratory. The tendency to-day is to ignore the practical side in teaching, and this is specially noticeable in our universities. The student of to-day will be the practicing doctor of to-morrow, but

one would rather think that he was intended to be a research student in a laboratory to the end of his days. That is one reason why the old family doctor was such a boon to the community. The modern man, crammed with theoretical knowledge and laboratory methods, is far behind his elder, if less erudite confrère, so far as the practical side of his profession is concerned. He knows how to write an ethical prescription, and he pulls his patient through without subjecting him to laboratory analysis or experimenting on his stomach with drugs whose actions are probably at the most but vague and uncertain. The modern and so-called "up-to-date" practitioner cannot write an ethical prescription, cannot weigh up the pulse without complicated instruments, cannot recognize a fractured collar-bone without the help of the X-rays, and cannot diagnose an early tuberculous lesion until the patient has been "screened" by a radiologist. We doubt if all this makes for progress. It may impress the public, but it creates in our minds a feeling of diffidence and uncertainty.

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#### LIST OF PROPOSED ADDITIONS AND DELETIONS TO THE NATIONAL FORMULARY.

At the recent meeting of the National Formulary Committee, it was decided to submit to the medical and pharmaceutical journals a list of the official titles which had been proposed for deletion in the revision of the work and likewise a list of titles which so far have been proposed for admission in the Revised Formulary. These are published as a tentative proposition for the information of the pharmaceutical and medical professions in the hope that those interested will express their opinions thereon either through the medium of the JOURNAL or directly to the Chairman of the Committee, Wilbur L. Scoville, P. O. Box 488, Detroit, Mich. The final decision of the Committee will depend very largely upon these expressions of approval or disapproval of the proposed actions.

In addition to the list of proposed additions, the Committee solicits from dental and veterinary associations a list of articles of sufficient use in these branches of medicine to merit recognition by standard formulas in the National Formulary. The Committee welcomes suggestions from any source.

PROPOSED DELETIONS FROM THE N. F.

Acetum Opii  
Collodium Tigllii  
Collodium Iodi  
Collodium Iodoformi  
Cordiale Rubi Fructus  
Decoctum Sarsaparillae Compositum  
Elixir Aurantii Amari  
Elixir Bismuthi  
Elixir Calcii Bromidi  
Elixir Calcii Hypophosphitis  
Elixir Calcii Lactophosphatis  
Elixir Cinchonae Alkaloidorum, Ferri et Pepsini  
Elixir Cinchonae Alkaloidorum, et Hyposphosphitum  
Elixir Cinchonae Alkaloidorum, Ferri et Bismuthi  
Elixir Cinchonae Alkaloidorum, Ferri, Bismuthi et Strychninae  
Elixir Cinchonae Alkaloidorum, Ferri et Calcii Lactophosphatis  
Elixir Corydalis Compositum  
Elixir Ferri Hypophosphitis  
Elixir Ferri Lactatis  
Elixir Formatum  
Elixir Formatum Compositum  
Elixir Humuli  
Elixir Hypophosphitum  
Elixir Hypophosphitum et Ferri  
Elixir Lithii Citratis  
Elixir Pepsini et Ferri  
Elixir Rubi Compositum  
Elixir Salicylatis  
Elixir Strychninae Valeratis  
Elixir Viburni Prunifolii  
Elixir Zinci Valeratis  
Emulsum Olei Morrhuæ cum Calcii Lactophosphate  
Emulsum Olei Morrhuæ cum Calcii Phosphate  
Emulsum Olei Morrhuæ cum Pruno Virginiana  
Emulsum Olei Morrhuæ cum Vitello  
Emulsum Olei Ricini  
Emulsum Petrolati  
Fluidextractum Cinchonae Aquosum  
Fluidextractum Coffeae  
Fluidextractum Conii  
Fluidextractum Corydalis  
Fluidextractum Helianthemii  
Fluidextractum Paracoto  
Fluidextractum Petroselini Radicis  
Fluidextractum Verbenæ  
Gelatinum Chondri

Glyceritum Vitelli  
Glyceritum Guaiaci  
Glyceritum Tragacanthae  
Glycerogelatinum Acidi Salicylici  
Glycerogelatinum Iodoformi  
Glycerogelatinum Zinci Durum  
Glycerogelatinum Zinci Molle  
Gossypium Stypticum  
Infusum Brayerae  
Iodoformum Aromatisatum  
Linimentum Ammonii Iodidi  
Linimentum Tiglli  
Linimentum Tiglli Compositum  
Liquor Alumini Acetico Tartratis  
Liquor Bismuthi  
Liquor Bromi  
Liquor Ferri Citratis  
Liquor Ferri Hypophosphitis  
Liquor Ferri Nitratis  
Liquor Ferri Protochloridi  
Liquor Ferri Oxysulphatis  
Liquor Magnesii Sulphatis Effervescens  
Liquor Pancreatini  
Liquor Pepsini  
Liquor Pepsini Aromaticus  
Liquor Phosphori  
Liquor Sodii Arsenatis, Pearson  
Liquor Sodii Citro-Tartratis Effervescens  
Liquor Strychninae Acetatis  
Liquor Zinci et Alumini Compositus  
Liquor Zinci et Ferri Compositus  
Magma Ferri Hydroxidi  
Massa Copaibae  
Mistura Carminativa  
Mistura Opii et Sassafras  
Mistura Guaiaci  
Mistura Olei Picis  
Mistura Pectoralis, Stokes  
Mulla Acidi Salicylici  
Mulla Creosoti Salicylata  
Mulla Hydrargyri Chloridi Corrosivi  
Mulla Zinci  
Oleatum Aconitinae  
Oleatum Atropinae  
Oleatum Cocainae  
Oleatum Quininae  
Oleatum Veratrinae  
Petroxylins—Too many. Which can be spared?



Petroxolinum Betanaphtholis  
Petroxolinum Cadinum  
Petroxolinum Chloroformi Camphoratum  
Petroxolinum Creosoti  
Petroxolinum Eucalyptolis  
Petroxolinum Guaiacolis  
Petroxolinum Hydrargyri  
Petroxolinum Iodi  
Petroxolinum Iodi Dilutum  
Petroxolinum Iodoformi  
Petroxolinum Liquidum  
Petroxolinum Mentholis  
Petroxolinum Methylis Salicylatis  
Petroxolinum Phenolis  
Petroxolinum Phenolis Camphoratum  
Petroxolinum Picis  
Petroxolinum Spissum  
Petroxolinum Sulphuratum  
Petroxolinum Sulphuratum Compositum  
Petroxolinum Terebinthinae Laricis  
Phenol Iodatum  
Pilulae Antimonii Compositae  
Pilulae Antidyspepticae  
Pilulae Colodynthidis Compositae  
Pilulae Colodynthidis et Hyoscyami  
Pilulae Colodynthidis et Posophylli  
Pilulae Ferri, Quininae, Strychninae et Arseni Fortiores  
Pilulae Glycerytis Nitratis  
Potassa cum Calce  
Pulvis Gambir Compositus  
Pulvis Kino et Opii Compositus  
Sal. Lithii Citratis Effervescens Compositum  
Sal. Potassii Bromidi Effervescens Compositum  
Sal. Vichyanum Factitium Effervescens cum Lithio  
Soda cum Calce  
Sodii Boro-Benzoeas  
Succus Citri et Pepsinum  
Syrupus Althææ  
Syrupus Calcii Hydrochlorophosphatis  
Syrupus Calcii Hypophosphitis  
Syrupus Calcii Iodidi  
Syrupus Calcii Lactophosphatis et Ferri  
Syrupus Cimicifugae Compositus  
Syrupus Codeinae  
Syrupus Ferri et Mangani Iodidi  
Syrupus Ferri Hypophosphitis  
Syrupus Ferri Lactophosphatis  
Syrupus Ferri Protochloridi

Syrupus Morphinae et Acaciae  
 Syrupus Sodii Hypophosphitis  
 Syrupus Stillingiae Compositus  
 Tinctura Amara  
 Tinctura Aromatica  
 Tinctura Caramellis  
 Tinctura Ergota Ammoniata  
 Tinctura Iodi Decolorata  
 Tinctura Kino et Opii Composita  
 Tinctura Paracoto  
 Tinctura Pectoralis  
 Tinctura Rhei et Gentinae  
 Tinctura Zedoariae Amara  
 Trochisci Carbonis Ligni  
 Trochisci Gambir  
 Trochisci Menthae Piperitae  
 Unguentum Picis Compositum  
 Unguentum Plumbi Iodidi  
 Unguentum Veratrinae  
 Unguentum Zinci Stearatis  
 Vinum Aurantii Compositum  
 Vinum Carnis  
 Vinum Carnis et Ferri  
 Vinum Ferri  
 Vinum Fraxini  
 Vinum Pepsini  
 Vinum Picis  
 Vinum Pruni Virginianae  
 Vinum Pruni Virginianae Ferratum  
 Vinum Rhei Compositum

#### PROPOSED ADDITIONS.

Compound Digestive Elixir—modified  
 Compound Mustard Ointment  
 Compound Capsicum Ointment  
 Compound Syrup of Thyme  
 Suspension (or Emulsion) of Benzyl Benzoate  
 Ampoules

## CONTROL OF PATENT MEDICINES IN UNITED KINGDOM.\*

BY CONSUL GENERAL ROBERT P. SKINNER,

LONDON, APRIL 24, 1920.

The British Minister of Health has appointed a committee to advise on legislative and administrative measures to be taken for the control of the quality and authenticity of therapeutic sub-

\* From *Commerce Reports*, June 1, 1920.

stances or patent medicines offered for sale to the public, which cannot be tested adequately by direct chemical means. Some of the most distinguished professional people of Great Britain have been named upon the committee, which will consider in the first instance the report of a select committee of the House of Commons on patent medicines. This committee issued a report in August, 1914, summarizing the legal position in regard to patent medicines, as follows:

"For all practical purposes British law is powerless to prevent any person from procuring any drug or taking any mixture, whether potent or without any therapeutical activity whatever (so long as it does not contain a scheduled poison), advertising it in any decent terms as a cure for any disease or ailment, recommending it by bogus testimonials and the invented opinions and facsimile signatures of fictitious physicians, and selling it under any name he chooses, on the payment of a small stamp duty, for any price he can persuade a credulous public to pay."

Principal Recommendations of the Committee.—The principal recommendations of the committee were:

"That the administration of the law governing the advertisement and sale of patent and secret medicines be combined under one department of the State—the Ministry of Health when created, and until then the local government board.

"That the manufacturers, proprietors, and importers of such medicines be registered.

"That an exact and complete analysis of every remedy, including medicated wines, with a full statement of the claims made for them, be furnished to the department.

"That a special court or commission be constituted with power to permit or prohibit in the public interest, or on the ground of non-compliance with the law, the sale and advertisement of any remedy; and that the commission be a judicial authority, such as a metropolitan police magistrate sitting with two assessors, one appointed by the department and the other by some such body as the London Chamber of Commerce.

"That the advertisement and sale (except the sale by a doctor's order) of medicines purporting to cure the following diseases, be prohibited: Cancer, consumption, lupus, deafness, diabetes, paralysis, fits, epilepsy, locomotor ataxia, Bright's disease, rupture (without operation or appliances).

"That it be a breach of the law to use fictitious testimonials, or to promise to return money paid if a cure is not effected."

THE CANADIAN AND BRITISH LAWS RELATING TO  
CHEMICAL PATENTS\*

BY A. E. MACRAE.

In the present Canadian Act there is no restriction on the nature of the composition of matter which may be patented, except that it must be new and useful and the result of invention. The same conditions exist in the United States and did exist in Great Britain until a very recent date, when a new Patents and Designs Bill, which was introduced in the British House of Commons, in November, 1917, became law. This Bill passed the House of Commons without debate, discussion, or division, and by it, I understand, products of chemical processes or intended for food or for medicinal or surgical purposes may not be claimed in a patent application but only the process. That is, specifications relating to an article or substance made by chemical processes or intended for medicinal or surgical use may contain claims for the process of manufacture only and not for the substance or composition of matter. Some other countries also refuse patent protection on similar compositions. Germany, Austria, Japan, and Russia refuse to grant patents on foods, medicines, or chemical products, and in Switzerland neither the product nor the process of making them may be patented. Sweden will patent processes of making foods or medicines but not the product. Denmark will not patent medicines, articles of food, or processes of making articles of food. France, Italy, and Spain refuse patents on medicines and pharmaceutical preparations of all kinds.

\* *Journal of the Society of Chemical Industry*, Vol. 39, May 31, 1920, No. 10, p. 177r.

## NEW FACTS REGARDING OPIUM ALKALOIDS.\*

In a series of investigations on the pharmacology of opium alkaloids Macht emphasized that these compounds could be grouped into two distinct categories; in doing this he<sup>1</sup> defined more clearly the work of Pal, Straub, Sahli, and others. One of the categories, the piperidin-phenanthrene group, of which morphine is the principal member, includes substances that stimulate the contractions

\* From *Jour. Amer. Med. Assoc.*, July 17, 1920.

<sup>1</sup> Macht, D. I.: "Action of Opium Alkaloids," *J. Pharmacol. & Exper. Therap.*, 7: 339, 1915.

and increase the tonus of smooth muscle. The second, or benzyl-isoquinolin group, of which papaverin is the conspicuous member, inhibits the contractions and lowers the tonus of the same active tissue. It was through the discriminating pharmacologic analysis that attention became prominently directed to the inhibitory effect of benzyl alcohol and its derivatives, so that they have found some recognition in therapy as antispasmodics. On the other hand, Straub's so-called morphine reaction, consisting in a peculiar stiffening or bending backward or curling of the tails of mice which have received doses of morphine, can now be explained as due to the spasms of the sphincters of the anus and bladder provoked by the alkaloid in question. As the morphine molecule includes both piperidin and phenanthrene groups, Macht<sup>2</sup> has undertaken to ascertain the effect of these groups separately on smooth muscle. The upshot of the research has been to demonstrate the comparative inertness of phenanthrene, whereas piperidin is found to be a powerful stimulant of this contractile tissue, suitable doses causing an increase in the rate and strength of its contractions and an increase in its tonicity. Macht asserts that this interesting effect of piperidin on smooth muscle has never before been described. Its possible significance deserves further consideration.

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## ENGLISH DRIED-FLOWER INDUSTRY.

BY ALFRED NUTTING,

CLERK IN AMERICAN CONSULATE GENERAL, LONDON.

In consequence of the shortage during the war of medicinal herbs, an association of women in Suffolk started the systematic collection of such plants. From 1916 to 1918 belladonna, henbane and foxglove were the chief herbs handled. Last year the demand for these fell off, but in their place arose a request for sweet-smelling herbs and flowers, and it is reported that during the current year collections thereof for the perfumery trade are being organized throughout the county of Suffolk. The new scheme is under the supervision of women botanical experts. It is stated that this rural industry has already resulted in considerable pecuniary benefit to East Anglian villagers, who have been instructed in the proper method of collecting. During the current month the picking of fresh heads of cowslips commences, cowslips being used for sachets

<sup>2</sup> Macht, D. I.: "A Pharmacodynamic Analysis of Straub's Morphine Reaction," *J. Pharmacol. & Exper. Therap.*, 15: 243 (May), 1920.

and potpourri as well as a cure for sleeplessness; broom and elder flowers will follow and many others.

A mill at Blackenham purchases the collections and prepares them for the market. The prices per pound at the mill for such dried flowers are: Cowslips (heads only), 2 cents; broom flowers, 6 cents; elder heads, 1 cent, with florets picked off, 5 cents; lime, 8 cents; mullein and mallow, 8 cents; bergamot (flowers without calyx), 12 cents; lavender—on stalks, 12 cents, rubbed off stalks, 61 cents; dark red peony petals, 10 cents; dark red rose petals, 6 cents; red field poppy petals, 8 cents; mullein leaves, 2 cents; raspberry leaves, 1 cent; sage, mint, balm, agrimony, and woodruff (whole herbs), 2 cents. Thyme brings 36 cents per 14 pounds. (From *Commerce Reports*, May 10, 1920.)

## ELECTRICAL STERILIZATION OF MILK.\*

BY ALFRED NUTTING,

CLERK IN AMERICAN CONSULATE GENERAL, LONDON, ENGLAND, MAY 12, 1920.

A special report has just been issued by the British Medical Research Committee, dealing with the destruction of bacteria in milk by electricity. In the introduction it is pointed out that the earliest description of an electrical method having this purpose in view was published by the Liverpool (England) Corporation in 1915, the investigator being Prof. J. Martin Beattie, of the University of Liverpool. Subsequently independent trials of the method were undertaken at Birmingham, and the opinion of the committee is that these latter experiments, while supporting the practical results obtained at Liverpool, did not entirely prove whether the electrical current in the method adopted had a directly bactericidal action or acted as a thermal agent. Sir Oliver Lodge, inclined to the latter view.

The report itself has been prepared by Profs. Beattie and Lewis, both of Liverpool University, and enumerates the results of 15 experiments under varying conditions, with different degrees of current and with several qualities of milk, as well as showing two types of apparatus used. The final conclusions arrived at by the investigators are:

Milk can be rendered free from *B. coli* and *B. tuberculosis* by the new electrical method described without raising the temperature

\* From *Commerce Reports*, June 10, 1920.

higher than 63 degrees or 64 degrees C. This temperature effect is very short in duration and in itself is not the principal factor in the destruction of the bacteria. Though the milk is not sterilized in the strict sense of the word, yet the percentage reduction of the bacteria taken over a period of a fortnight is 99.93. The keeping power of the milk is considerably increased.

The taste of the milk is not altered, and so far as careful chemical examination can determine the properties of the milk are not in any way impaired. The milk can accurately be described as "raw milk" free from pathogenetic bacteria.

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### LICORICE INDUSTRY IN SICILY.\*

BY COMMERCIAL ATTACHÉ ALFRED P. DENNIS,

ROME, ITALY.

Licorice root forms an important minor article of Italian export to the United States. Figures covering prepared licorice are not available; but shipments of licorice root for the year 1919 amounted to 1,304 metric tons to the United States alone, out of a total exportation of 1,899 metric tons. The bulk of Italian licorice is grown in Calabria, the southernmost Province of Italy, and the prepared licorice is manufactured in the city of Messina.

The bulk of the manufactured licorice is exported to England and to Denmark the present quotation being £20 per quintal (220 pounds) f. o. b. vessel, Messina, for blocks of five kilos each, while stick licorice is quoted at £30. The boxes of 130 kilos capacity, in which the product is packed for export, are expensive, costing about 20 lire each.

The macerated pulp fiber left over from the process of production is now employed as a fertilizer, but experiments are being made for the conversion of this fiber into a tough quality of wrapping paper.

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### CURRENT LITERATURE.

#### MEDICAL AND PHARMACEUTICAL NOTES.

ANILINE POISONING—Max Nassauer (*Zeitschrift für angewandte Chemie*, 1919, xxxii (I), 333-335) states that a malignant tumor or cancer of the bladder occurs as an occupational disease among work-

\* From *Commerce Reports*, June 9, 1920.

men who are exposed to the vapors of aniline. During a period of twenty-three years, from 25 to 30 per cent. of the tumors of the bladder, which came to operation at the surgical clinic of the University at Frankfurt am Main, were caused by aniline. The vapors of aniline are inhaled highly diluted with air; their effect on the bladder is slowly cumulative; the first symptoms of the cancer appear, on the average, when the workman has been employed in the factory for sixteen years. In order to reduce the danger to a minimum, the plant must be constructed of impervious materials and be amply ventilated; the evolved gases must be purified before their escape into the atmosphere; closed apparatus must be used; liquid raw materials and products must be handled with compressed air, solids by mechanical devices. Ample bathing facilities must be provided and used at the end of each day's work. Clean work clothes and wooden shoes must be worn daily, and gas-masks and rubber gloves must be used when necessary. The urine of the workmen should be examined at frequent intervals. (From *Jour. Franklin Institute*, May, 1920.)

**SODIUM CHLORIDE AS ANTIDOTE FOR STRYCHNINE.**—Giribaldi cites authors who claim that sodium chloride renders certain poisons less soluble, and describes research on rabbits and dogs which demonstrated that a strong solution of salt has a certain action in this line. The sodium chloride must follow the strychnine in less than five minutes, either by the mouth or subcutaneously, for any effect to be apparent. (*Gazzetta degli Ospedali e delle Cliniche*, Milan, December 11, 1919, 40, No. 99; through *Jour. Amer. Med. Assoc.*, May 8, 1920.)

**ARSENICAL POISONING FOLLOWING USE OF ARSPHENAMIN.**—Fifty-eight cases of delayed poisoning following the administration of arsphenamin and mercury were observed by the authors in military hospitals and in private practice. Forty-seven of these showed symptoms referable to the liver, namely, jaundice, decreased digestive power and liver atrophy. Eight of these were fatal and at necropsy showed marked atrophy of the liver. Dermatitis occurred in eight cases. Five were severe with marked exfoliation. Peripheral neuritis was observed in two cases. Albuminuria was present in over 50 per cent. of the cases. Edema was found in two cases. The onset of the symptoms seldom occurred until five weeks after the administration of arsphenamin had ceased. The earliest symp-



toms of arsphenamin poisoning of the liver were, bile in the urine, albuminuria, loss of appetite and jaundice. Dermatitis with atrophy of the liver occurred in one patient who received arsenic in the form of Fowler's solution, 5 minims, three times daily, for five months. (*Canadian Medical Assoc. Jour.*, Toronto, April, 1920, 10, No. 4; through *Jour. Amer. Med. Assoc.*, May 15, 1920.)

DELAYED ARSENICAL POISONING FOLLOWING USE OF ARSPHEN-AMIN.—Fifty-eight cases of delayed arsenical poisoning following the use of arsphenamin preparations are reported by Strathy and his associates. Eight of these were fatal, being the first of the series to come under observation. The remaining fifty patients made a slow but otherwise satisfactory convalescence. The greatest number of doses of arsphenamin given in the fatal cases was eleven, the least four. The greatest amount administered, where it was possible to obtain records, was 6.95 Gm., the least amount 2.2 Gm. The average time of onset of symptoms after the last dose was forty-one days, the longest interval forty-eight days, the shortest eighteen days. The symptoms in every case were similar. The jaundice on onset was rapidly followed by nausea, epigastric pain, stupor, hematemesis, delirium and death. Four of the patients were wildly delirious. In all cases tested the urine contained bile, and in nearly all cases albumin as well. The blood picture was not characteristic. The hemoglobin and red cells were not much reduced. The leukocytes varied in number from 14,000 to 34,000 per cubic millimeter, and the polymorphonuclear leukocytes from 50 to 80 per cent. The greatest number of doses of arsphenamin given in the non-fatal cases was fourteen, the least two. The average time of onset of symptoms was forty-five days, the longest interval 180 days, the shortest three days. Thirty-nine of the patients were admitted for jaundice, eight for dermatitis, two for nephritis, and one for general debility. Jaundice followed dermatitis in one patient, and two other cases of dermatitis were followed by peripheral neuritis. Coated tongue, poor appetite, epigastric distress, abdominal distension, headache, general malaise, and loss of weight were noted throughout the group. Albuminuria was present in twenty-eight cases, bile salts in thirty-five cases, increased urobilin and urobilinogen in sixteen cases, leucin and tyrosin were never found. Jaundice was present in all of the fatal group and thirty-nine of the non-fatal group. (From *Lancet*, London; through *Jour. Amer. Med. Assoc.*, May 22, 1920.)

*Excessive Sweating of the Feet.*—Lopez discusses this subject from the military standpoint, and his success in curing plantar hyperhydrosis in soldiers with a dusting powder consisting of 60 parts alum and 40 parts talcum powder. This reduced or checked completely the excessive sweating, eliminated the bad odor, and prevented maceration, etc., from the sweat, while saving the shoes from constant moisture. He ascribes the cause of the hyperhydrosis and certain vasomotor phenomena, chilblains, varices, haemorrhoids, and similar minor disturbances to some general toxic action, and thinks that incipient, attenuated tuberculosis is responsible for this in many cases. He says that general treatment by the Argentine method of extremely minute doses of tuberculin may be worth a trial, or with Ferran's antialpha serotherapy or vaccine. (From *Semana Medica*, Buenos Aires, Mar. 25, 1920; through *Jour. Amer. Med. Assoc.*, Aug. 14, 1920.)

*The Excretion of Quinine.*—As having a bearing on the recent discussions on the value and method of administration of quinine, a report made to the War Office by M. Nierenstein and cited in the *Lancet* (1920, 1, 1126, May 22) is of some importance. This investigator finds that half of the quinine administered is excreted by way of the urine, while the remainder is metabolized into quinine and haemoquinic acid, both of which are found in the urine. The tests for these bodies are qualitative and quantitative, those recommended being Herapath's elaborated by Ramsden and Lipkin for the former and Barratt and Yorke's for the latter. Haemoquinic acid is constantly present in blackwater fever, in much larger quantities than in the urine of ordinary malarial patients. There is no variation in the proportion excreted if the dose is from 20 to 70 grains daily. A dose of over 30 grains, which raised the unchanged quinine in the urine above 11 grains per liter, is apt to cause albuminuria. A variation of the preparations administered does not alter the proportion of quinine excreted unchanged. (Editorial from *The Prescriber*, August, 1920.)

*Mercurochrome-220 in Ophthalmia Neonatorum.*—The new anti-septic *Mercurochrome-220*, has been tried in ophthalmia neonatorum by C. A. Clapp and M. G. Martin, who issue a preliminary report (*Jour. Amer. Med. Assoc.*, 74: 1224, 1920, May 1). They describe four cases, in all of which the infection completely disappeared under treatment with this drug. A 2 per cent. solution was used. The

authors comment most favorably on its penetrating power and its germicidal action on the gonococcus; they also remark that it is practically non-irritating and harmless to the eyes, only a slight burning effect being experienced during the first few seconds. The red stain is to some extent a drawback, but it is no more objectionable than argyrol in this respect, and will not produce a permanent stain, as occasionally happens with the silver preparations. (From *The Prescriber*, August, 1920.)

*Phenyl-methyl Carbinol: A New Local Anaesthetic.*—In our issue of May, 1920, p. 212, reference was made to benzyl carbinol, or rose oil, as a local anaesthetic. A. M. Hjort and C. E. Kaufmann (*Jour. Pharm. and Exp. Ther.*, 15: 129, 1920, Apr.) have conducted experiments with its isomer phenyl-methyl carbinol. They find it to be a more potent local anaesthetic on the rabbit's cornea and in the human skin than either its isomer rose oil or their homologue benzyl alcohol, but not in proportion to its greater toxic action. The relative instability of the  $\alpha$ -phenethylol offers further objection to its practical application. It is suggested that the increased physiological action may be due to the presence of the asymmetric carbon atom. (From *The Prescriber*, August, 1920.)

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### CORRESPONDENCE.

BROOKLYN, N. Y., August 31, 1920.

*"Credit to Whom Credit is Due."*

MY DEAR BERINGER:

Would thank you for the following correction, A. J. PH. in connection with my paper "Pharmaceutical Events 1870," published in the August number:

In the article on Simpson and the Introduction of Chloroform on p. 572 the statement is made:

*This account is taken from the author's lectures.*

Somehow the typist forgot the succeeding line:

*and Victor Robinson's fascinating book "Pathfinders in Medicine."*

I, as one, believe in giving "credit to whom credit is due" and expect to be treated the same way.

Fraternally yours,

OTTO RAUBENHEIMER, PH.M.

## BOOK REVIEWS.

PHARMACEUTICAL BACTERIOLOGY. By A. Schneider, M.D., Ph.D.  
Published by P. Blakiston's Son & Co.

This, the second edition, was made necessary by the rapid changes and advances in the science of bacteriology.

In the first chapter, the author gives the history of the introduction of this science in pharmacy throughout the United States, together with the various problems in bacteriology directly connected with the practice of pharmacy. A number of references of benefit to students and pharmacists, who may desire further information, are listed at the close of the chapter.

Chapter II deals with the complete history of bacteriology from the days of Hippocrates (300 B.C.) to the present day. The entire time is divided into five periods. A list of useful works of reference in bacteriology and related topics is given here.

Chapters I and II of this edition are almost identical with the corresponding chapters of Edition I.

Chapter III, one of the newly added chapters, deals with some of the important hypotheses and theories regarding the origin of bacteria and micro-organisms in general.

New additions have been added to the text of Chapter III of the first edition, resulting in the production of Chapter IV of this edition. Herein is found the physiological and morphological characteristics of bacteria, together with a general classification of microbes.

Chapter V is identical to Chapter IV of the first edition. Information regarding the range and distribution of microbes, written on two pages, makes this chapter a small one. It could just as readily have been incorporated in one of the foregoing chapters.

Chapter VI is the first data of interest to the practical pharmacist seeking information relating to bacteriology. This chapter is almost identical with Chapter V of the previous edition, published in 1912. To the advanced pharmacy student the information available is clear. To the average pharmacist or to the two-year pharmacy student a more detailed and explicit explanation is necessary. Here is found a description of the containers used, with methods of cleaning and preparing them for sterilization. A consideration of the preparation, sterilization and titration of culture media is also available, together with methods for making cultures,

bacterial counts, staining solutions, and methods for examining bacteria.

Chapter VII, a newly added chapter, gives detailed information regarding the biological relationships of bacteria with a general introduction to the phenomena of Symbiosis. This chapter is very interesting and of considerable value to bacteriologists and advanced students, but the average pharmacist would have little use for this information.

Chapter VIII treats more fully (than the corresponding chapter in the previous edition) of bacteria found in industries. The information treats of the function of bacteria in agriculture, together with interesting data relating to the bacteria and methods of examining bacteria in milk, in the dairy industry, in water supplies, in the tanning industry, in cider making, and bacterial pest exterminators.

Chapter IX is a newly added chapter on ferments and fermentation.

Chapter X, on immunity and immunizing agents, has been enlarged.

The manufacture and use of sera and vaccines and other biological products are found in Chapter XI.

Adenology, the science which treats of glands, is contained in Chapter XII, together with methods for the preservations and storage of biological products. Adenology, though of value to the pharmacist, due to his interest in glandular extracts, is not a bacteriological topic, even though recent investigations have demonstrated that the activity of the glands are directly connected with the process of immunization.

Chapter XIII gives extensive information relating to yeasts and moulds.

In Chapter XIV is found data relating to protozoa in disease. Here is another chapter dealing with information other than bacteriology. The data given is brief and incomplete. Mention should be made in the preface that Chapters XI and XIII contain information of importance to pharmacists and only indirectly related to bacteriology.

Chapter XV, on disinfectants and disinfection, food preservation and insecticides, is incomplete. There is very little that has been added to the identical chapter of edition I, published in 1912, though considerable new materials and information on these topics

have been introduced within these eight years. No mention is made of the newer antiseptics commonly prescribed and called for.

Chapter XVI treats of sterilization and disinfection in the pharmacy. The information here is identical with the same data published in the first edition. The information given is practical and interesting. Though ampul making has advanced, the author has little to add to the methods of sterilizing medicaments in ampuls. It would be interesting to learn where the table, naming the sterilizing temperature for solutions in ampuls was obtained. There has been very little information regarding experimentation along these lines in American pharmacy. Such work requires considerable time and research, but it is urgently needed. A large amount of this data seems to have been traveling from book to book with no one standing directly responsible for the information given.

Chapter XVII treats of the causes and prevention of the common communicable diseases. A small portion of the information here is far advanced for the pharmacist. A specific example is the attempt to explain briefly the Wassermann test.

In the last chapter (Chapter XVIII) will be found an outline of microscopical and bacteriological work together with numerous suggestions on a micro-analytical and bacteriological laboratory.

Another chapter should have been added giving information regarding the more commonly observed bacteria together with their illustrations. This is important.

The book, taken as a whole, is of value not only to advanced pharmacy students, but probably more so to bacteriologists in general, and it is a question whether the author would not gain more by naming the book "General Bacteriology," with special mention in the preface of certain facts to pharmacists, rather than "Pharmaceutical Bacteriology." To the average two-year pharmacy student, only a few of the chapters in the book are of value. The others treat of the more advanced information relating to bacteriology. It is on this account that the previous suggestion is raised.

LOUIS GERSHENFELD

STANDARDS AND TESTS FOR REAGENT CHEMICALS. By Benjamin L. Murray, member of American Chemical Society, Chemical Society (London), American Electrochemical Society, Societe de Chimie Industrielle, Society Chemical Industry, etc., etc. 385 pages. Price, \$3.00 net. D. Van Nostrand Co., New York, 1920.

This volume, full of important information, takes up physical and chemical reagents, organic and inorganic, in alphabetical order, giving descriptions of the physical properties, action of light and air, precautions to be observed in storing, statements of uses, maximum limits of impurities and methods of testing; the last generally includes a quantitative assay. The percentage purity of inorganic chemicals are not always in accord with the U. S. P. IX.

The following quotations are from the preface: "The statements of the 'Maximum Limits of Impurities,' so often recurring throughout the book, are not the amounts of impurities present, but are the maxima permissible in chemicals suitable for miscellaneous reagent purposes. The reagents of the market are frequently, if not generally, well below these maxima. The percentage figures in which the above limits are stated were in part determined by the customary quantitative tests, and to this extent are accurate; in part by qualitative tests in which the reactions in unknowns are compared with those in knowns." "The tests will insure good reagents even though the stated percentages of impurities may not be entirely correct."

Tests for impurities in most cases are made directly with solutions of the chemicals and only in comparatively few cases is the precaution taken to remove substances which may interfere with the particular test. The test for calcium is made in ammoniacal solution by addition of ammonium oxalate; the test for aluminum is made by addition of ammonia, consequently both of these metals will yield precipitates in the calcium test; the test for heavy metals will serve to indicate individual metals, but if mixtures are present the test for the metals comprising the mixture must be more or less uncertain. These statements are made because in the "Maximum Limits of Impurities" the percentages of individual metals are given and these figures were probably obtained by adding known solutions of each metal to the chemical reagent and then proceeding with the test. In many cases the production of a color or turbidity proves the presence or absence of the impurity; more detail should be given as to the amount of reagent to be added so that the final volume of the test will be known, also as to the dimensions of the vessel in which the test is judged. In connection with the tests for arsenic it may be of interest to mention that Marsh's and Bettendorf's tests only are used. Any one using chemical reagents will find this book very valuable.

FRANK X. MOERK.

ANNALS OF THE MISSOURI BOTANICAL GARDEN Vol. 6, No. 4, 1919.

*The Thelephoraceae of North America XI.*—E. A. Burt discusses the generic characters of *Tulasnella*, *Veluticeps*, *Mycobonia*, *Epithele* and *Lachnocladium*, as well as the characteristics of three species of *Tulasnella*, two species of *Veluticeps*, two species of *Mycobonia*, two species of *Epithele*, and 12 species of *Lachnocladium*. Fifteen figures and one clear plate of nine figures accompany the article.

*A Subterranean Alga Flora.* By G. T. Moore and J. L. Karrer.—The authors, in this valuable investigation, inoculated ten different series of culture bottles with soil samples from various parts of the Missouri Botanical Garden, Woods Hole and Santa Ana, California. The cultures were taken at varying depths up to one meter and the varieties of soil examined were heavy clay, loose clay, sand, sandy alkali, sandy gravel and humus. The subterranean cultures were obtained from places where the soil had not been disturbed for at least a number of years, in order that the algal growths obtained would represent those typical of subterranean conditions and not merely surface infections.

They tabulate their results in nine tables, Series A being omitted in their tabulations. The authors, however, mention that *Proto-derma viride* and *Anabaena* appeared in the latter. From the records in these tables the authors conclude:

1. That there exists a subterranean algal flora, independent of the nature of the soil and the locality.
2. That *Proto-derma viride* occurs constantly at the greatest depth.
3. That, as pointed out by Esmarch, the flora undoubtedly originated from the surface flora.
4. That the greatest growth in the cultures was at a depth of 5–60 cm. A list of seventeen different algae found in the cultures is given, together with a statement of the greatest depth at which each occurred.

*Culture Experiments with Melampsora in Japan.* Three figs. By Takashi Matsumoto.—This article comprises supplementary notes on cultural experiments with *Melampsora* on species of *Salix* and *Populus*. It is a sequel to the writer's first article which was reported in Japan in 1915.

HEBER W. YOUNGKEN.

PROCEEDINGS OF THE NATIONAL WHOLESALE DRUGGISTS' ASSOCIATION'S 45TH ANNUAL MEETING AT NEW ORLEANS, LA., NOVEMBER 3RD TO 7TH, 1919.—This official record of the Annual Meeting



of the N. W. D. A., held at the Hotel Grunewald, New Orleans, is presented in a well printed volume of 599 pages. It contains the addresses, reports and various actions taken at the Annual Meeting. The report of the Committee on Memorial is illustrated by a miniature portrait of each of the deceased members.

The various important reports are well worthy of careful perusal. Undoubtedly, under existing conditions, that on legislation claims first attention.

Through its various committees, this Association is, from time to time, presenting reports of great value on the subjects of Fire Insurance, Transportation, Adulterations, Trade Marks, Business Methods, etc., which are well worthy of careful study, by the various branches of the drug trade.

The banquet served on the evening of November 6th, is fully described. John W. Durr, of Montgomery, Ala., acted as the toastmaster, and addresses were made by officers and prominent guests.

The closing pages of the volume contain the certificate of incorporation, Constitution and By-Laws, and a well prepared index. The volume throughout bespeaks the solid character of the Association, and this is fully sustained by the published list of members.

G. M. B.

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## THE EXAMINATION OF CHINESE CRUDE CAMPHOR.\*

By E. R. DOVEY, A.R.C.Sc., A.I.C.

In the examination of crude camphor, the estimations usually required are those of non-volatile matter (or dirt), moisture, and oil, and the sum of these impurities subtracted from 100 per cent. is supposed to represent the camphor present. The moisture may be conveniently estimated by the calcium carbide method, allowing three hours for the evolution of gas, and the dirt by the residue left after volatilizing a weighed portion of camphor.

So far as is known to the writer, no reliable method for the estimation of camphor oil in crude camphor has been published, other than the melting-point method given in Allen's "Commercial Organic Analysis," Vol. iv, p. 197.

As this laboratory was called upon to examine a considerable number of Chinese crude camphors, the following method worked

\* From *The Analyst*, June, 1920.

out here may be of interest: The moisture is first estimated on the well-mixed sample, then 100 Gm., weighed to the nearest 0.1 Gm., are transferred to a press and pressed between two layers of lint. The press designed for this work has a steel cylinder 2 inches in diameter, and 6 inches deep, and is furnished with a movable perforated bottom plate. The piston is operated by a strong screw thread. The sample is allowed to remain in the press under pressure for fifteen minutes, at the end of which time it is carefully removed and the pressed cake weighed, any camphor adhering to the lint being carefully brushed off and added to the cake. From the loss in weight the amount of water plus oil expressed is found.

The moisture is then estimated on the pressed cake, and from the difference between the result and the original moisture the amount of water expressed is found, and, by difference, the amount of oil in the expressed liquid is found.

It is then assumed that the water still remaining in the pressed cake is associated with as much oil as that in the expressed liquid, and the total oil calculated on that basis. The accuracy of this assumption may be open to question, but, with a good press, very little moisture remains in the cake, while the m. p. of the pressed camphor usually indicates a fairly high degree of purity.

GOVERNMENT LABORATORY,  
HONGKONG.

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# THE AMERICAN JOURNAL OF PHARMACY



OCTOBER, 1920

EDITORIAL.

## COMPREHENSIVE PHARMACEUTICAL RESEARCH.

One of the great lessons taught by the world war was the dependence of the industries upon the sciences. The tide of battle was swayed by the preponderance of scientific knowledge and its skillful application to the destruction of life and property. The destiny of nations was jeopardized and wavered in the balance until this advantage of the enemy became fully recognized and with feverish haste the latent resources, the inventive ingenuity and scientific knowledge of the allies, were mobilized into coördinated research.

The National Research Council was hastily organized in 1916 for the purpose of stimulating and coördinating research necessitated by the war problems and for a period this had the financial support of the National Government. In 1918, by executive order of the President of the United States, it was reorganized as a permanent body and the secretary now states that "its essential purpose is the promotion of scientific research and of the application and dissemination of scientific knowledge for the benefit of the national strength and well being."

While the conduct of the war to a favorable conclusion was pending as the largest contract ever undertaken by this nation, research as applied to the problems of the war, necessarily from the very urgency, received paramount consideration and held a prominent position in the public view. The value of scientific research appeared to be indelibly impressed upon government officials and many public spirited citizens. Now that the problems of war no longer hold the pre-eminent position in the public interest, it is in order to note how deep and how lasting have been the impressions made by this great lesson growing out of the exigencies of the war.

The National Research Council, we are advised, "is no longer government supported and while maintaining a close coöperation with the government scientific bureaus, it is in no sense a government bureau but is now entirely supported by other than government sources, and is entirely controlled by its own representatively selected membership and democratically chosen officers." The problems of peace are no less important than are those of war. The application of scientific principles to the development of the peaceful arts and industries assures a great increase in the productiveness, efficiency and wealth of the Nation and a larger measure of comfort and enjoyment to the individual. This means higher ideals in literature, art, industry and commerce, in fact in all proper lines of human effort, and far more toward the world's progress and happiness than can ever come from the destruction, devastation, destitution and misery resulting from the dire necessities of war.

The world has had its surfeit of war with the profligate waste of life and property. The time has now come for the inauguration of grand national movements by which scientific investigations shall be thoroughly and systematically organized and coördinated and the results obtained be applied intensely to the benefit of mankind. The conservation of our national resources and the stimulating of our industrial development in accordance with the highest scientific attainments, should now become our national problems. It is gratifying to observe that in England there has been established by government grant the Committee for Scientific and Industrial Research and in our own country that the National Research Council has been permanently reorganized and to note the efforts and the progress so far made by these movements.

Pharmacists are concerned that the necessity for the organization of a comprehensive plan for pharmaceutical research be recognized and that the value to mankind of the results that may be obtained thereby, shall be fully appreciated. So far the importance of the drug industry has not been publicly understood, and the insufficiency of our knowledge concerning nearly every potent medicine dispensed by pharmacists has not been given the consideration that is due either by the government authorities or by the philanthropists who have created research endowments or by those subsequently in control of such establishments. It is only too evident, that neither of these two national research foundations has yet given the serious consideration to the formulating of a plan for comprehensive phar-

maceutical research that, we are convinced, is merited by the importance of the subject and its benefit to the national strength and well being.

It is known that the National Research Council has named as one of its divisions "the medical sciences," but we are not advised that pharmacy is to be organized as a subdivision thereof or that pharmaceutical research is to be given special recognition or encouragement. We unhesitatingly assert that the thorough study of the numerous products supplied by pharmacists and the processes employed in the preparation of medicines, will open boundless fields for exploration with innumerable research problems the possibilities of which and the value thereof to mankind cannot be pre-estimated. We are firm in our conviction that "the sum of scientific knowledge for the benefit of the national strength and well being," acquired thereby will hold no secondary place.

Mr. W. Kirby, in his presidential address before the British Pharmaceutical Conference last year, fully set forth the need for pharmaceutical research and the duty of the government to encourage and foster this. At the recent meeting of the American Pharmaceutical Association, in responding to the address of Dr. C. E. McClung representing the Division of Medical Sciences of the National Research Council, Prof. John Uri Lloyd eloquently portrayed how the supplies of the pharmacist were drawn from every portion of the Natural Kingdoms and from all quarters of the globe and that these products alone presented an endless variety of problems of the utmost importance for investigation for the advancement of human knowledge to the benefit of mankind.

These representative leaders in pharmaceutic thought in their respective countries, comprehend fully the importance of comprehensive pharmaceutical research as a national asset and likewise its direct influence upon the development of professional pharmacy. If the entire membership of the pharmaceutical and drug trade organizations were imbued with the same spirit and comprehensive view of the subject, the internal indifference would give way to earnest, enthusiastic support and a national pharmaceutical research endowment would be promptly established and in its functioning maintain the proper professional status of pharmacy and demonstrate the sphere of usefulness of pharmacy to society and the service that it renders.

Pharmacy is not medicine nor is it chemistry, although closely

allied with each of these professions and coördinating with both in their respective spheres. It performs a distinct duty to the public and must be accorded recognition as a separate vocation with its own problems peculiar to its field of service. We cannot expect that the leader in medicine shall understand or that he will be especially concerned with the specific problems of pharmacy nor can we expect the chemist to have the viewpoint of the pharmacist. *It would be very unfortunate to all interests concerned to have pharmaceutical research controlled by others than pharmacists.* The propositions for pharmaceutic research that have heretofore emanated from these outside sources have but served to demonstrate the insufficiency of the view and the failure to comprehend the extensive fields awaiting organized pharmaceutical research. The plan of one of the proposed pharmaceutic research funds was limited to investigations of the pharmacologic actions of new synthetic chemicals for which therapeutic claims are made.

Any plan for pharmaceutical research that will have the hope of success must be a comprehensive scheme outlined by pharmacists who have a broad conception of the possibilities and a vision that will embrace every branch of pharmaceutical activity and co-ordinate the contemplated investigations with those of allied professions and industries. The acceptance of any other than a distinct and individual plan of research for pharmacy controlled and managed by pharmacists, must prove futile and wasteful of funds, time and energy. Pharmacy must energetically work out its own solution of the research question and incidentally its own destiny as the scientific progress and professional status of our vocation will depend in a large measure upon the manner in which this is done. In England as well as in the United States the importance of research is being recognized and there appears to be a growing sentiment that the pharmaceutical and drug trade organizations must form their own research association. Current literature amply demonstrates the need and the pages of the AMERICAN JOURNAL OF PHARMACY alone furnish numerous problems that call for further scientific investigation.

G. M. B.

## RHUS VENENATA DC.

BY HEBER W. YOUNGKEN, PH.D., AND GEORGE A. SLOTHOWER, B.Sc. B.A.P.

PHILADELPHIA, PA.

Five poisonous species of *Rhus* plants are common to the United States and Canada, namely: *Rhus toxicodendron* L., *Rhus venenata* DC, *Rhus diversiloba* Torr. and Gray, *Rhus succedanea* L, and *Rhus vernicifera* DC.

Commercially, *Rhus vernicifera*, *Rhus succedanea*, and to some extent, *Rhus venenata*, yield a lac which is of value in the making of the famous Japan varnishes.

*Rhus toxicodendron* was official in the sixth and seventh editions of the U. S. P. Its use in medicine at the present time is in the main limited to the practice of homeopathy, where it is used in nervous disorders and dermatotherapy. Rost and Gilg<sup>1</sup> make mention of it as having been used in the treatment of cancer.

There are probably no other plants in existence which cause as much human distress and suffering as *Rhus toxicodendron* and *Rhus venenata*.

Many substances are referred to in the literature as causing the dermatitis produced by these plants. They include a vapor, gas, volatile alkaloid, volatile acid, infection by bacteria, glucoside, non-volatile acid, resin, polyhydric phenol and a non-volatile oil.

That the poisonous substance was a non-volatile oil, which resinifies on exposure to the atmosphere, was discovered by Pfaff<sup>2</sup> who found it to exist in all parts of the plant.

As to how this non-volatile oil comes in contact with individuals, the consensus of opinion seems to be that the winds and domestic animals carry the pollen grains and hairs. Pfaff and Schwalbe<sup>3</sup> found the pollen grains and hairs to contain the poisonous substance. On the other hand, Rost and Gilg,<sup>1</sup> in a very extensive work, were unable to find the poison in the hairs and pollen from these plants.

In this investigation we shall undertake to inquire into the histological nature of the stems and leaves of *Rhus venenata* and make observations on its poisonous constituent.

The specimens used in this work were collected near Atco, New Jersey, in July of 1919, and allowed to dry. The Martindale Herbarium of the Philadelphia College of Pharmacy and Science was consulted and proved of considerable value.

## DESCRIPTION OF PLANT.

*Rhus venenata* De Candolle, family *Anacardiaceae*, is commonly known as swamp-sumac, poison sumac, poison elder and poison dogwood. The latter synonym must not be confused with the flowering dogwood, which is a member of the *Cornaceae* family.

It is a shrub possessing a slender clustered stem, which sometimes takes a tree-like form, reaching to a considerable height. The stem is brittle, showing for the most part a pithy region internally. The leaves are 7-13 foliate, with slender reddish green petioles. The leaflets are obovate, oblong, dark green and glossy on the ventral surface, paler on the dorsal side, and without marginal teeth. The midrib and veins are prominent. The flowers are dioecious and are in narrow axillary panicles, yellowish green to white in color. The petals are slightly reflexed. The stamens appear nearly twice as long as the petals. The fruit is a smooth, white drupe, often remaining on the branches until spring. The leaf scars are prominent, alternate and of a somewhat crescent shape. The bark on young stems is mottled with conspicuous lenticels.

## HISTOLOGY OF STEM.

We find the epidermis to be composed of a single layer of epidermal cells with a thick outer cuticle. The subepidermal region shows a couple of layers of cork cells, more or less tangentially elongated. The cortex region is compact in nature and consists for the most part of sclerosed parenchyma. Numerous rosette, aggregate crystals of calcium oxalate are found in this region. Resin canals are present in the primary cortex, which, according to Sole-reder<sup>4</sup> is common in the *Rhus venenata*. The structure of the pericycle varies according to the age of the plant. In the older stems isolated groups of sclerenchyma fibers occur usually in the form of adjacent arcs. The convex side of each of these is directed towards the exterior. The inner concave side of each arches over a dome-shaped phloem in the centre of which is a single resin canal. In younger stems the arcs (strands) of sclerenchyma fibers are joined with each other by means of sclerosed parenchyma. In this way the pericycle constitutes a continuous ring of stereomatic structure, which covers the phloem-containing resin canals as a single band. A zone of cambium cells, more or less collapsed, is found separating the phloem region from the xylem. The prosenchyma forming the structure of the wood has simple and bordered pores. The



medullary-rays are usually one and two cells wide, with four cells as the maximum width. As stated by Solereder,<sup>4</sup> the resin canals, which are characteristic for the plants of the Anacardiaceae, often extend from the bast region and penetrate into the medullary region,

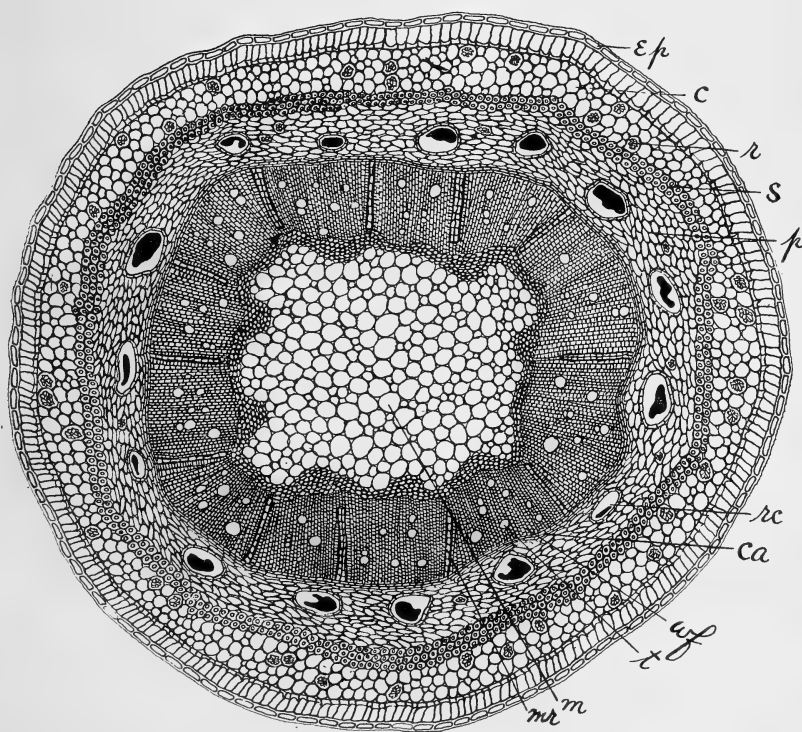


Fig. 1.—Transverse section of young stem of *Rhus venenata* DC. Epidermis (*ep*); cortex (*c*); rosette crystals of calcium oxalate (*r*); continuous ring of stereomatic tissue in pericycle (*s*); phloem (*p*); resin canals (*rc*); cambium (*ca*); xylem (*x*); wood fibers (*wf*); and tracheae (*t*) of the xylem; medullary rays (*mr*); pith (*m*).

where they end blindly. The canals are narrow-branching vessels filled with a dark reddish brown substance of a resinous nature. This substance responded to the cyanin test for resin. It did not react to the chemical tests for gummy lignin as noted by Youngken<sup>5</sup>

in stems of the *Myricaceae*. On treatment with alcoholic potash solution the resinous material combines with it to form a nigrescent compound. This reaction is characteristic<sup>3</sup> of the poisonous substance causing the dermatitis produced by poisonous species of *Rhus* plants. The pith consists of thin-walled parenchyma cells with an occasional duct.

#### HISTOLOGY OF LEAF.

The lamina is of dorsiventral structure. A layer of thin-walled cells forms the epidermis of the ventral surface. In the mesophyll region there is a ventral stratum of palisade tissue and a dorsal pneumatic tissue of large roundish cells, which often contain rosette crystals of calcium oxalate. Stomata lacking subsidiary cells and raised a little above the adjoining epidermis are present in the dorsal epidermal region. The resin canals, which were present in the fibro-vascular bundles of the stem, also accompany the vascular bundles

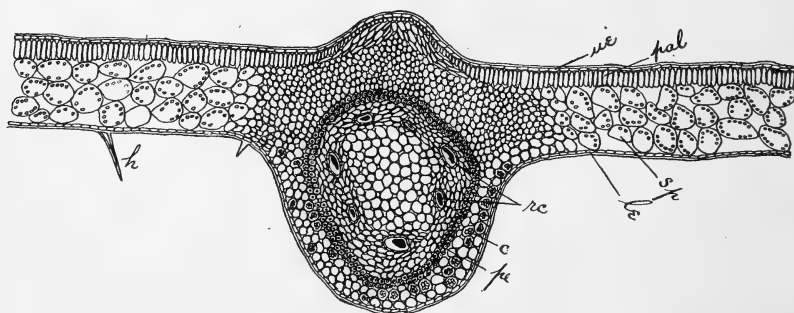


Fig. 2.—Transverse section through midrib and portion of lamina of *Rhus venenata*. Upper epidermis (ue); palisade parenchyma (pal); spongy parenchyma (sp); lower epidermis (le); resin canals (rc); rosette crystals of calcium oxalate (c); pericyclic fibers (pe); hairs (h).

of the leaf in both the larger and smaller veins. Collenchyma tissue is present in the dorsal region of the midrib. Non-glandular unicellular and uniseriate hairs are found in the dorsal region. They are present in greater number along the veins. Many contain the "resinous substance" of Schwalbe, which responds to the nigrescent reaction when treated with alcoholic potash solution. Schwalbe<sup>3</sup> accounts for the presence of this resinous material in the hairs of *Rhus toxicodendron* as a product of osmosis from the neighboring lacticiferous vessels containing the resin. In the *Rhus venenata* resin canals are found to be the conducting vessels. As the resin

canals were not found to penetrate the mesophyll region, the presence of the resin in the hairs may be due to osmosis. We are inclined to believe it may be a direct product of the protoplasm, which the authors hope to report in a later article.

In the approximate chemical analysis the dried leaves and petiole were passed through a number 60-mesh sieve. This yielded a dark green-colored powder with a very peculiar, offensive odor.

The sample being in a dry state, oxidation and change of character of some constituents most likely took place, which must be considered.

On ignition the powder yielded 6.5% ash content. The residue was grayish brown and had an alkaline reaction. Traces of potas-

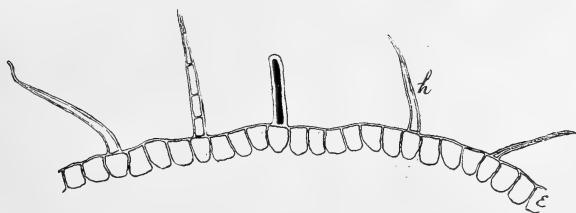


Fig. 3.—Vertical view of portion of dorsal epidermis of *R. venenata* lamina. Epidermal cells (*e*); non-glandular hairs (*h*).

sium, chlorides, phosphates and sulphates were found in the ash. Nitrogen was determined by the Kjeldahl method. The presence of nitrates and nitrites could not be found.

Four extractions were carried out by the Soxhlet continuous extraction method. Each extraction extended over a period of 3 days, allowing the solvent to macerate the sample during the nights.

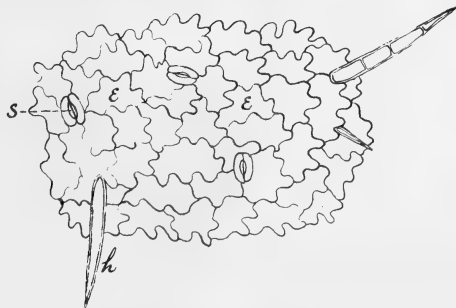


Fig. 4.—Surface view of dorsal epidermis of *R. venenata* lamina showing hairs (*h*); wavy walled epidermal cells (*e*); and stomata (*s*).

A good grade of low-boiling petroleum ether was used in the first extraction. In this solvent ethereal and non-volatile fixed oil was obtained, as well as a great amount of chlorophyll. On standing a white waxy-like substance separated out of the petroleum extract.

By spontaneous evaporation of a portion of the petroleum extract a yellowish brown, oily residue was obtained. This residue, when taken up with neutral alcohol, is neutral in reaction.

The alcoholic solution of the residue was optically inactive, which Pfaff states is true of the non-volatile oil causing the dermatitis.

The residue from the petroleum ether extract, when taken up with alcoholic potash solution, can be saponified. No glycerin is liberated.

To confirm, practically, that the poisonous principle was obtained in the petroleum ether extract, the same was applied to the inner forearm with a piece of cotton and allowed to remain. In twenty-four hours inflammation with violent itching occurred and in thirty hours vesication had taken place.

An alcoholic solution of the residue, when treated with a solution of lead acetate, will cause precipitation of the lead salt of the oil to take place. By treatment of this lead compound with hydrogen sulphide, Stevens was able to isolate the oil from the *Rhus toxicodendron*.

As irritation is often due to precipitation of proteins, experiments were made to precipitate egg and blood albumen from 0.5 per cent. solutions, by treatment with an alcoholic solution of the residue from the petroleum ether extract. Negative results were obtained. More extensive experimentation with oil obtained from fresh plants is hoped to be carried out in a continued article by the authors.

In the presence of fixed oil, alkaloids are often extracted simultaneously by petroleum ether, but no alkaloids could be extracted from the stems or leaves of this plant.

The second extraction was with ether. This was not carried out until all the petroleum ether had evaporated from the marc.

The ether extract was dark red-brown in color, which yielded a residue of the same color. When taken up with neutral alcohol the reaction was unchanged. Precipitation took place when the ether extract was treated with lead acetate solution. An alcoholic solution of the ether residue will precipitate a resin out of solution

when poured into water. No poisonous principle was found in the ether extract when applied to the inner forearm.

The alcoholic extraction which was carried out after all the ether evaporated yielded a yellowish brown solution in which tests for tannin were positive. No poisonous constituent was found in the alcohol extract.

The water extract gave tests for mucilaginous substances when mixed with alcohol by precipitating them out of solution. Fehling's solution was reduced by the aqueous extract.

At the present time no reliable form of treatment for the dermatitis caused by these plants is known. What will often effect relief in some cases will be obstinate and often assist perverse conditions to develop in other individuals.

That immunity may play a part is believed by some scientific workers, but this generalization is more common among the laity.

Cases of *Rhus* poisoning in the winter months are frequently met with, and are accounted for by the presence of the hairs on the stems and branches throughout the entire year.

Generally the hairs penetrate into the sudoriferous and sebaceous glands. This observation is corroborated by the fact that parts of the skin perspiring easily are affected most frequently by the poisonous principle.

Whether this non-volatile oil is taken up by the blood to form toxic substances is a field for biological research in connection with the comparative toxicity of the oil from *Rhus toxicodendron* and *Rhus venenata*, respectively.

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## THE PHARMACOLOGICAL ACTION OF ADONIS VERNALIS.

BY JAMES M. SCHMIDT, M.D.

FROM THE BIOLOGICAL LABORATORY OF THE UPJOHN COMPANY.

*Adonis Vernalis*, or Pheasant's eye, is named among the drugs which possess the power of stimulating the heart. Its position in the group of digitaloid drugs is dependent upon a rather limited amount of experimental work, and a few instances of its clinical use. In the following we review the previous work upon the plant and add the results of our own investigation.

The literature with reference to *Adonis Vernalis* may be briefly reviewed as follows:

In 1882, Cervello<sup>1</sup> reported on the pharmacology of adonidin, the "glucosidal" active principle of adonis. This report consisted chiefly of the clinical results of its administration and a demonstration of its action upon the heart and blood pressure in mammals. His conclusion states that adonis is very similar to digitalis, in that it slows the heart, and increases the blood pressure in mammals; and that toxic doses will stop the frog's heart in strong systole with the auricles widely dilated, just as is the case in a digitalis heart.

Fucklemann<sup>2</sup> in 1911, reported on the chemistry and pharmacology of the drug, also giving the results in a few cases of its clinical application.

During 1913, Slovtzov<sup>3</sup> concluded that adonis regulates the action of the heart, slows its rate, and strengthens its beat; but that it increases the rate of the heart in cold blooded animals.

Chevalier<sup>4</sup> stated that adonis is like squills and not like digitalis, and that its principle effect is a stimulation of the kidneys. During the same year, 1913, Fucklemann<sup>5</sup> said that adonidin possessed digitaloid effects.

In the year 1914, Mercier<sup>6</sup> repeated Fucklemann's experiments and concluded that "adonidic acid" contained in adonis, had a paralyzing and contracting action upon the heart muscle, and is very similar to the digitonin in digitalis. Also in 1914, Roch and Cramer<sup>7</sup> claimed that large doses of adonis were insufficient in cardiac diseases.

In 1918, Heyl, Hart and Schmidt<sup>8</sup> published the results of a thorough chemical examination of adonis leaves. They analyzed various extracts of adonis and compared with these the toxicity as determined by the one-hour frog assay.

In the following work an attempt has been made to compare

galenical adonis extracts with digitalis and the other cardiac stimulants, both as to strength and to action.

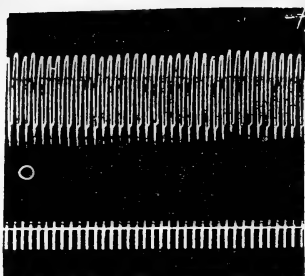
#### THE ACTION OF ADONIS UPON THE FROG'S HEART.

Frogs, of the type *Rana Pipiens*, which have received toxic doses of adonis, show but slight irritation. Their attitude is rather one of depression until shortly before their heart stops beating, when they show evidence of some discomfort. The ability to control voluntary movements, however, often remains after the heart has stopped, for having been injected with a toxic dose of adonis, the frog may hop about normally, and make every effort to avoid being caught; but after pithing and opening its thorax, it will have a heart which is stopped in permanent systole. This would tend to show that the drug acts more upon the heart than upon the central nervous system in general.

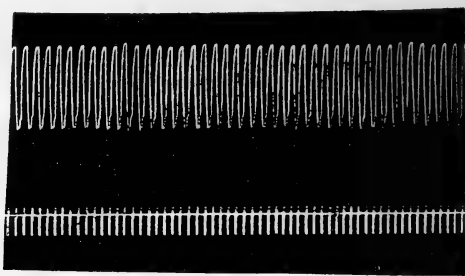
The following table is a typical chart of a frog's heart poisoned with adonis.

18 gm. frog, brain pithed and heart exposed.		
Time.	Rate of beat per minute.	Remarks.
1:49	33	
1:51		2 cc. of adonis injected into the lymph sac of of the leg.
1:54	33	
1:55	31	
1:58	29	The ventricle is paler and contracts more strongly.
2:00	23	
2:03	22	Auricles and ventricles beating strongly and in unison.
2:05	20	This is the rate of both auricles and ventri- cles.
2:10	14	Ventricles have stopped, this is auricular rate.
2:12		Auricles are still beating, though irregularly, the ventricle is contracted firmly and does not beat.
2:15		The auricle has stopped beating and is widely dilated. The ventricle is small and pale in color.

Although the systolic effect of the drug is evident from careful examination during several autopsies, it is demonstrated in the tracings as 1-C, by the increased distance between the mark of the lever and the base line. In many instances there is some increase in

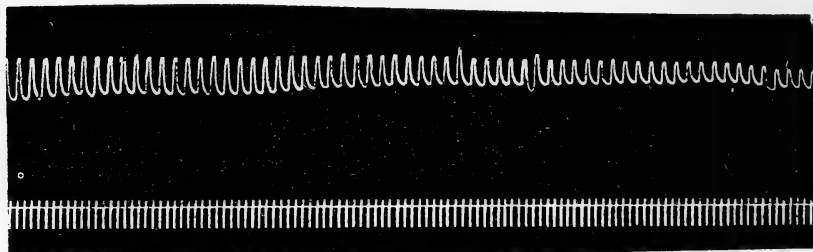


Tracing 1-A. From a normally beating frog's heart.



Tracing 1-B. From a frog's heart shortly after the application of adonis; showing a slightly slower rate of beat.

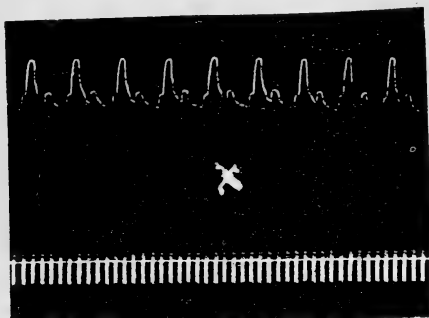
dilatation shown shortly after the application of the drug; this is always immediately followed by a lessened dilatation, as the lever rises higher and higher each succeeding diastole. Since the systolic contraction cannot raise the lever higher even by its increased



Tracing 1-C. The same tracing later.

strength, the excursions become gradually smaller until the heart finally stops. Records of the heart taken in this manner frequently show a one to two rhythm between the auricles and the ventricles in the latter stages of poisoning (see tracing 1-D); this indicates that adonis decreases the power of conduction between the auricles and the ventricles, in the same manner as does digitalis. The tracings 1-A, B, C, are very typical of the effect of adonis upon the heart's rate of beat. The heart is always slowed until it reaches the toxic stage when it becomes rapid and irregular. When the frog's heart has been stopped by adonis, it presents a very characteristic picture, namely, that the ventricular walls are firmly contracted so that they appear quite pale in color, the auricles being widely





Tracing 1-D. Showing the one to two rhythms often displayed after the application of adonis. The time is marked in seconds, the lever moves upwards in systole and downwards in diastole.

dilated and filled with dark unoxygenated blood. In short the hearts appear to be typical digitalis hearts.

Since the frog hearts which had been poisoned with adonis, presented the typical digitalis picture, it seemed reasonable that adonis could be assayed by the one-hour frog method which is official for digitalis.

#### THE ASSAY OF ADONIS.

The information with regard to adonis has been derived from work done upon two lots of the drug, which we have called Drug A and Drug B. Alcoholic tinctures were made from these drugs at different times and they were assayed as follows:

#### DRUG A.

Per cent. of alcohol in the menstruum used.	Toxicity, or the minimum systolic dose (M. S. D.) per gram of frog.
95	0.0043 cc.
95	0.0043 cc.
80	0.0033 cc.
70	0.0033 cc.
60	0.0040 cc.
50	0.0027 cc.

This makes the average toxicity 0.0036 cc. per gram of frog.

## DRUG B.

Per cent. of alcohol in the      Toxicity, or the M. S. D. per gram of frog.  
menstruum used.

95	0.0055 cc.
95	0.0045 cc.
50	0.00315 cc.
50	0.0043 cc.

The average toxicity of Drug B is 0.0043 cc.

From these results the average toxicity of Drug A is greater than that of Drug B. A total average for both drugs would be about 0.004 cc. of a tincture. In these assays the resistance of the frogs was taken into consideration; each lot was assayed against ouabain, as is ordinarily done in the assay of any of the heart tonics.

A tincture of adonis possessing a toxicity of 0.004 cc. per gm. of frog, was also assayed with guinea pigs, according to the manner followed in the twelve hour guinea pig assay of the heart tonics.<sup>9</sup> The pigs poisoned in this way, showed no peculiarly characteristic symptoms. They stand or lie quietly until near the very last, when they begin to struggle, and soon die. The assay is as follows:

Dose per Gm. of Pig.	Weight of Pig.	Actual Dose Given	Result in 12 Hours.
0.002 cc.	300 gms.	0.60 cc.	— living
0.003 cc.	340 "	1.02 cc.	— "
0.004 cc.	425 "	1.70 cc.	— "
0.005 cc.	330 "	1.65 cc.	— "
0.006 cc.	370 "	2.22 cc.	+ dead
0.007 cc.	415 "	2.905 cc.	+ "
0.008	425 "	3.40 cc.	+ "

Since we consider that a tincture of adonis, which assays 0.004 cc. by the one hour frog method is an average strength tincture; so we conclude that 0.006 cc. represents the average minimum lethal dose of adonis for guinea pigs.

## THE IRRITATING PROPERTIES OF ADONIS.

Digitoxin, a comparatively insoluble constituent of digitalis, is extremely irritating to the mucous membranes. Adonis, on the other hand, is soluble and produces but little irritation. Upon the injection of digitalis into the lymph sac of a frog, a certain amount of hyperaemia of the abdominal epidermis is frequently noticed, even though the alcohol had previously been most carefully removed. This was never noticed in the numerous assays of adonis. Neither do

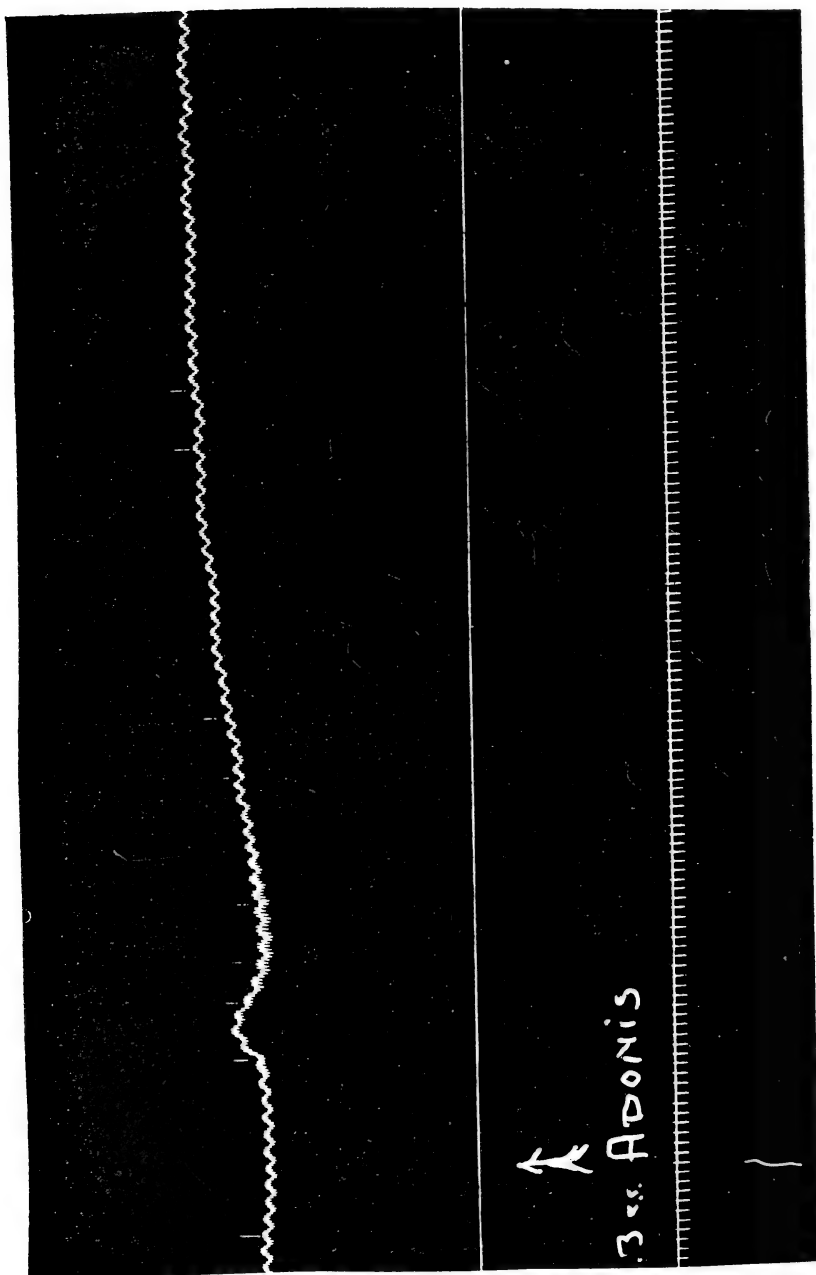
the frogs injected with adonis show the same amount of irritation as is so frequently seen in the digitalis frogs. They usually lie quietly until the very last, before showing any signs of discomfort.

One method of demonstrating the irritant properties of digitalis has been by perfusing frog hearts with physiological salt solution until they just stop beating.<sup>10</sup> Dilute digitalis preparations, either applied to the heart or introduced into the perfusing solution at this time, caused the heart to again start beating. Frog hearts treated in a similar manner with adonis, even with fairly strong solutions, could not be induced to again start beating. (Tracing 3-A and 3-B.)

Large doses of adonis administered orally to guinea pigs, rabbits and dogs, produced no vomiting and no apparent nausea, whereas the symptoms of digitalis poisoning are most constantly initiated by nausea and vomiting. As shown by Hatcher and Eggleston,<sup>11</sup> however, these symptoms may not be due to the irritation produced by the drug upon the gastric mucous membrane. They demonstrated that the intravenous injection of relatively small doses of digitalis to cats would produce emesis, even more readily than if administered orally, and that this action was probably due to its effect upon the central nervous system, rather than to any irritant properties that it might have upon the mucous membranes. They were able to produce emesis in dogs upon the intravenous injection of 0.5 mg. of digitoxin per kilo, while adonis required 65 mg. per kilo, or one hundred and thirty times as large a dose to produce the same result.<sup>12</sup> Whether the comparative lack of emetic properties possessed by adonis is due to the fact that it is non-irritating to the mucous membranes, or that it is unable to produce emesis by acting upon the medulla, the mere fact that it does not have the same amount of emetic action as digitalis might be a valuable therapeutic factor, for patients suffering from cardiac decompensation may suffer severely from gastric symptoms, and the administration of the emetic digitalis becomes most difficult.

#### THE ACTION OF ADONIS IN MAMMALS.

The blood pressure tracing shows three typical effects as taken from rabbits, following the intravenous injection of about one-half cc. of an average strength tincture of adonis. (Tracing 2.) There is an immediate rise in pressure, lasting on the average about five or ten seconds. After falling back to normal, there immediately



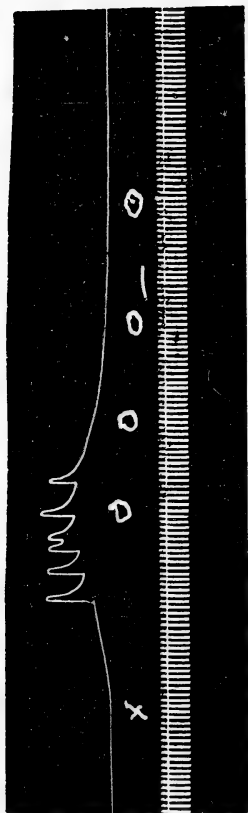
Tracing 2. This shows a typical blood pressure tracing as obtained from the insertion of a cannula into the carotid artery of a rabbit. In the course of one to two minutes the pressure returns to normal unless more adonis is given, in which case the heart passes into a typical toxic condition.

follows a more pronounced and more prolonged rise. In addition to this feature there is a marked slowing of the heart's rate, and frequently a clearly demonstrable increase in the pulse pressure. This increase occurs only in case there is a slowing of the heart's rate, and is the expected result upon the blood pressure of a strongly beating heart which is being slowed in rate, thus allowing the pressure to fall further between beats.

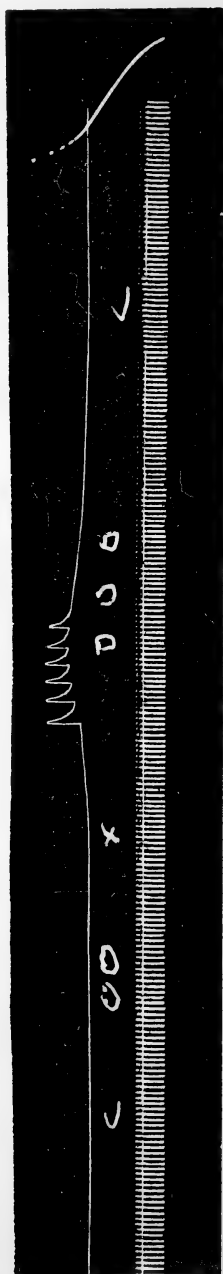
The effect of adonis upon the frog's heart has been previously discussed. Tracings 1-A, B, C, and D are typical of those produced by frog hearts whose action has been influenced by adonis. The hearts are markedly slowed in rate, show a decreased conduction between the auricles and the ventricles, and present an increase in the strength of the systolic contraction.

The reaction of the mammalian heart to adonis was studied in rabbits and dogs by means of the blood pressure tracings, and those obtained by the myocardiograph. The blood pressure record was taken from the carotid artery of rabbits, and shows a slowing of the rate of beat until a large amount of drug has been introduced into the blood stream, when the heart becomes irregular, many of its beats become inefficient, and there are large oscillations in the blood pressure resulting, until it finally falls as the heart stops beating. This heart, however, upon examination, is found widely dilated and in a diastolic condition.

In dogs, a myocardiographic record was made. This demonstrated that the rate of beat was slowed as in the other experiments, both auricles and ventricles showing this effect previous to the injection of sufficient adonis to produce an irregular or toxic action upon the heart. The increased systolic contraction becomes most evident here, being especially prominent in the ventricles. There is at times an increased dilatation, especially if the effect of the vagus nerve is not removed by atropine. Section of the vagi frequently has but slight effect, this factor however, being somewhat variable. Apparently adonis tends to a more peripheral stimulation of the vagus nerve than does digitalis; since in the experiments in which section of the vagi caused little change in the effects of adonis, there was a noticeable difference if atropine was administered. This consisted in less dilatation of the heart, instead of the increased dilatation usually produced by adonis; and also in a more rapid rate of beat instead of the slowed rate. This difference was not noticed when the same experiments were done with digitalis.



Tracing 3-A.



Tracing 3-B. These tracings were made in the usual manner, but the hearts were perfused with Ringer's solution for frogs until they stopped beating. At X a few drops of digitalis were placed upon the heart. At O it was washed with Ringer's solution. At < adonis was applied.

It has been noted that digitalis has two distinct actions upon the mammalian heart. The one is a slowing of its rate, produced by relatively small doses of digitalis, and removed by section of the vagus nerves or by the administration of atropine. Adonis in a like manner, in small doses, produces a slowing of the heart's rate, which in all cases can be removed by atropine. This action may be termed the beginning of the action of digitalis, or of adonis, and is purely a slowing of rate. Another phase of digitalis action is shown however, in cases of the administration of large doses of digitalis, especially in cases of fatal poisoning. This is evidenced by a more rapid rate of beat, and persists even after section of the vagi, or the injection of atropine. Cushny.<sup>10</sup> If the adonis action were to be compared with digitalis, it was considered necessary to compare this action also. Large doses of adonis given after removal of vagus control, show an increased rate of beat.

In order to determine the action of adonis upon the relative lengths of systole and diastole, tracings were taken from rapidly revolving drums and compared with the record of a tuning fork which vibrated at the rate of one hundred times per second. In this experiment frogs were used, and adonis applied to the exposed tissues immediately surrounding the heart. The following are the results taken from a single heart, but are typical of each experiment performed.

Measurements taken from the record made by the heart before adonis was applied gave the following results.

Duration of Systole in One Hun-	Duration of Diastole in One Hundredth
dredth of a Second.	of a Second.

Readings.	70	38
	72	38
	<u>69</u>	<u>38</u>
Average.	70	38

Measurements Taken One Minute after the Application of Adonis.

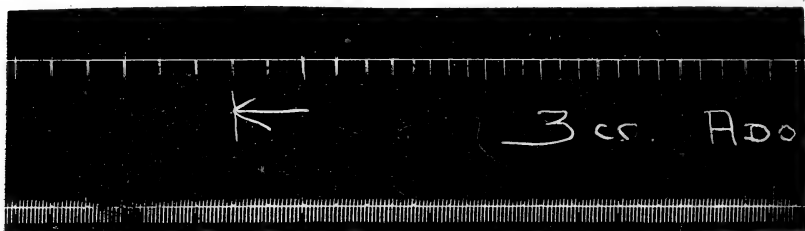
	82	55
	85	55
	82	50
		<u>49</u>
Average.	83	52

Measurements Taken Five Minutes after the Application of Adonis.

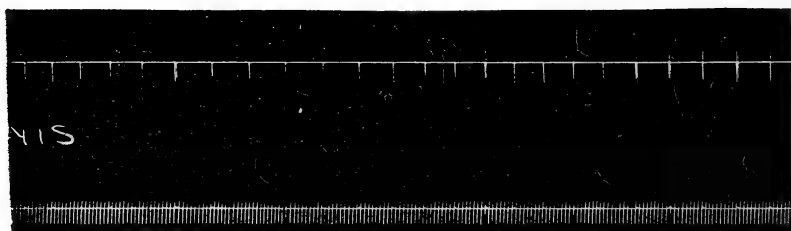
	71	64
	75	60
	<u>76</u>	
Average.	74	62

This shows an increase in the duration of both systole and diastole at first; the diastole being greatly increased in the later stages, while the systole is not quite so prolonged.

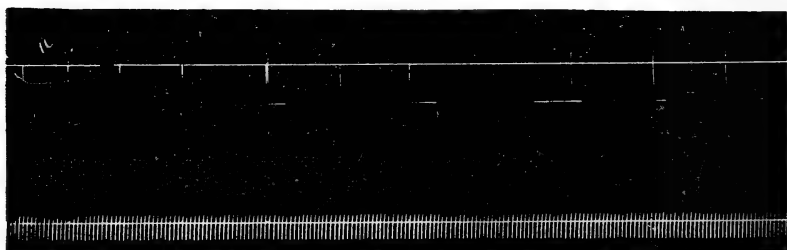
The effect of adonis on the peripheral blood vessels was determined by perfusing dilute solutions through the peripheral circulations of



Tracing 4-A.



Tracing 4-B.



Tracing 4-C.

Tracing 4-A. Shows the increased outflow from the venous cannula immediately following the administration of 0.3 cc. of adonis at arrow.

Tracing 4-B. A direct continuation of A, and shows a gradual slowing of the venous outflow, which becomes more marked in C.

frogs and rabbits. (Tracing 4.) In frogs a cannula was placed in the abdominal aorta and the drops recorded as they came from the median abdominal vein. A similar method was used in rabbits. The results in the two cases showed no variation. Ringer's solution was first perfused through, and after a normal or steady rate was ob-



tained, about a half mil. of alcohol-free adonis was introduced into the perfusing stream without producing an increase in pressure, and the effect recorded upon a drum, by means of an electrical drop recorder. As the result of this, there is shown at first a slight but very evident slowing of outflow. This is quickly followed by a more rapid output, and then as the drug continues to act, the drops come out more and more slowly. This demonstrates a temporary dilatation of the blood vessels, which at first will cause a slowing of the outflow, but as the perfusing solution continues to flow through the dilated vessels, the outflow is quickly increased. If larger amounts of adonis are placed in the perfusing solution, this first dilatation cannot be demonstrated, and even though small amounts of a dilute adonis are used, this preliminary dilatation is soon followed by a gradual and prolonged constriction of the vessels, so that the output of the perfusing solution from the vein is greatly decreased.

Experiments were carried out in exactly the same manner using digitalis, strophanthus, and squills. These drugs all produced the same effects in character, though strophanthus very evidently produces less effect upon the peripheral blood vessels than do digitalis or squills, and adonis gives results much more closely simulating digitalis than strophanthus.

It is to be noticed that the result of the effect of adonis on the blood vessels is most strictly comparable to the blood pressure tracings. The initial fall in pressure may be attributed to a temporary vaso-dilation, and the prolonged rise in pressure to a vaso-constriction. R. Joseph<sup>12</sup>, gave small doses of the digitalis drugs and demonstrated that if they had an effect on the heart, that they also had an effect on the blood vessels. This statement seems somewhat doubtful, in view of the fact that we are able to produce a marked slowing of the heart rate without producing any change in the blood pressure. He does, however, find that the action of digitalis upon the blood vessels produces a dilatation as well as a constriction. He shows a dilatation occurring soon after the drug enters the blood stream, and lasting but a short time; while the constriction is more prominent and is more prolonged.

An attempt was made to determine the effect of adonis upon the kidneys. A cannula was placed in the ureters of a rabbit, and by means of a drop recorder a record of the urine outflow was obtained along with that of the blood pressure. While there was usually a demonstrable increase in the output of urine during the period following the action of adonis, still this action did not seem to present

the same degree of prominence which was present in the experiments in which digitalis was used.

#### CONCLUSIONS.

We conclude that *Adonis Vernalis* stimulates the heart in a manner very similar to digitalis; that it produces variations in blood pressure characterized by a rise, if large doses are administered, or by no pressure effect if the doses are relatively small; that the changes in pressure are caused mainly by the action of the drug upon the blood vessels; that it is less irritating than digitalis and possesses less tendency to produce a gastric disturbance; and that it possesses approximately the same strength as digitalis preparations made according to the official directions for a tincture or a fluidextract.

I wish to express my indebtedness to Dr. F. W. Heyl for many helpful suggestions during the preparation of this paper.

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- <sup>11</sup>*Jour. Pharm. Exp. Therap.*, 4, 113.
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#### INSECTS USED IN MEDICINE.

BY JOHN T. LLOYD, PH.D.,

CINCINNATI, OHIO.

That insects and their by-products play an important part in the economy of man is known to every layman. All appreciate the uses made of honey by civilized peoples and many know the still greater importance it holds in the diet of the savage who is unable to concentrate the dilute juices of plants to syrup or sugar. Many savage peoples also relish the fat larvae of certain insects, and thus the insects themselves play their part by breaking the

monotony of a scanty primitive diet. In the arts we all know that certain products of insects are of great importance—every household uses beeswax, every painter uses shellac—both are produced by insects. Perhaps however it is not so well known to the layman as to the physician that a few insects play an important rôle in the modern practice of medicine.

Chief among insects of medicinal value may be mentioned *Apis* (the honey bee) and *Cantharis* (a blister beetle). These almost alone from a host of insect preparations of ancient times retain their place in modern practice.

That a multitude of insects found their way into the practice of medicine during the medieval age seems to have been due not to their tried and proven therapeutic value, but to the fact that the people of the time were devoutly religious. They believed that the earth and all upon the earth were created to serve the interests of Man. Following this line of argument it was an easy matter for them to account for the Creator's purpose in making such important foods as wheat, fruit and vegetables but it sometimes became exceedingly difficult to find an ample reason for the creation of some of the lower forms of life. One has but to read some of the old volumes to realize to what absurd extremes men were driven to explain the Creator's wisdom in giving to Man some of the insects. For example according to the old authors, ants were made to set an example of industry to Man and lice were good because they kept him from sleeping too much and becoming lazy. Nevertheless, after taxing their ingenuity to the utmost, they seemed to be unable to find the reason for the creation of many insects. These they assigned to medicine, and it is likely that because they were thus assigned to medicine their therapeutic values were learned. If anyone doubts that small quantities of a certain insect can have a definite physiological reaction on the human body he has but to take the prescribed dose of *Apis* to be convinced, or if this be not, at hand let him try the sting of a bee.

That more insect remedies are not now used in the practice of medicine is due, possibly, rather to the objectionable form in which they were administered in the old prescriptions, than to the lack of value of the material. For example, what modern physician's patients would submit to swallowing a "spider wrapped in dough," or the "oil of angle-worms macerated a week in the sun?" If plant products, such as alkaloids and resins, have therapeutic value, why

should not some of the products of insects be likewise active? Not alone do the bodies of insects contain the ordinary products of animal metabolism, but many species have highly specialized glands peculiar to themselves, that manufacture and secrete complex chemical products. These, by some species, are used to attract the mate, by others to repel enemies, either by repugnance or as mechanical barriers. Everyone is familiar with the disagreeable odor of the "stink bug," and with the more pleasant odor of the bumble-bee—each peculiar to the species—and everyone who has handled great numbers of living insects must have noticed the large number of specialized secretions, in some species pleasant, in others disagreeable. Some secretions are oil-like liquids that cling to the insects, others are volatile vapors thrown into the faces of approaching enemies, others are waxes, or froth-like secretions. In all they are as distinct as are the products of plants, but the physiological reactions of nearly all of them are as yet untried.

This is but a general view of a subject that permits of most interesting detail extensions.

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### URINARY CASTS.\*

BY LOUIS GERSHENFELD, PH.M.

Urinary casts are, in most cases, derived from the renal tubes but occasionally casts obtained from the glands connected with the urinary tract, are met with. There are cases on record where casts of the larger urinary passages, most frequently of the ureter or urethra, have been found. These are not microscopic, but can be seen with the naked eye, measuring in some instances as long as 3 or 4 inches. The latter are usually derived from cases associated with tumors of the bladder or kidney. Renal casts are almost invariably associated with albumin, present or recently present in the urine; and, with few exceptions, they indicate some pathological change in the kidney. After severe exertion, however, or during some temporary irritation or congestion, they may be found in the urine. They remain intact for a considerable length of time in acid urine, but quickly lose their shape and disappear in alkaline urines. It is for this reason that the search for casts must be made carefully from a fresh sample, for urine, upon standing, frequently becomes alkaline in reaction.

\* Read at the annual meeting of the Pennsylvania Pharmaceutical Association, Harrisburg, June, 1920.

The diameter of the different types of casts show a characteristic uniformity. The sides are usually parallel, while at the two extremities one is either pointed or rounded, and the other is frequently broken across. The structure may otherwise be straight or convoluted, while the length varies considerably.

Though it is difficult at times to distinguish between the different varieties, casts have been classified, according to their microscopical characteristics as follows: hyaline casts; waxy or colloid casts; granular casts (fine and coarse); epithelial casts; fatty casts; blood casts; pigment casts; leukocyte, pus or purulent casts; fibrinous casts; bacterial casts; calcareous casts; ammonium urate casts; spermatic casts.

The source of the albuminous material, making up the composition of a cast, is not known. Some claim that they are the products from broken down epithelial cells, contrary to the belief of others, who think that they are abnormal secretions thrown off by diseased renal cells. Other investigators have formed the opinion that the blood plays an as yet unknown rôle in the production of these pathological substances.

Though their source is still in doubt, it is, however, the belief of most workers, that this albuminous product enters the uriniferous tubules in such a physical state, as to be capable of being easily molded. It is also held that they are formed in the straight tubules, and not in the convoluted tubes. The casts assume the shape of the tubule, retaining within their structure whatever substances were lying free, and then bend themselves up, or are forced to assume a wavy or convoluted shape, due to the obstacles they meet as they are forced out by the pressure of the urine. It is for this reason that the various forms are met with. There apparently seems to be no definite relationship between the number of casts present and the severity of a morbid process.

*Hyaline Casts.*—These are the most frequently observed casts, found in almost all kidney disorders, and occasionally in transitory conditions. They are straight or convoluted, transparent, homogeneous, and very delicate in structure. Their length and breadth vary, while their form may show marked variations. These casts are frequently coated more or less completely with albuminous débris or other granular material, such deposits giving a granular appearance to the casts. The impregnations commonly observed are various cells, either epithelium, erythrocytes, leukocytes or the

products of their disintegration, or non-organized constituents, as urates. Hyaline casts differ from cylindroids, which they so closely resemble:

1st. Tube casts do not form sharp angular bends, as found in cylindroids.

2nd. Cylindroids always exhibit a longitudinal striation, and are usually considerably longer.

3rd. Cylindroids do and hyaline casts do not give the mucin reaction (the production of coarsely granular turbidity (observed microscopically) on the addition of acetic acid).

*Waxy (or Colloid) Casts.*—The term waxy has been one of considerable misunderstanding and confusion. Colloid is a better term to use. The term waxy should only be used for those casts that possess a lardaceous or waxy composition. They give no precipitate with acetic acid, nor do they swell under the action of this acid. Their composition possesses all the characteristics of that widely discussed, ill-defined and yet unknown material, called by the name of colloid substance. It is thought that these casts are formed by an alteration of albuminoid material, produced by degeneration of renal epithelial cells. This accumulating in the tubules, probably gets mixed with other exudations from the blood vessels, and what is known as colloid casts result. It is on this account that these casts are found most frequently, associated with chronic renal diseases, and are usually indicative of serious lesions.

Colloid casts have a peculiar, dull, opaque appearance (being more opaque than the hyaline casts), always broader than the latter variety, frequently shorter, but may vary considerably in length, and are either longitudinally fissured and with more or less irregular broken ends. The borders are sharply defined and show indentations. Colloid casts of large diameter and length if present, can only be observed, providing great care is used in the treatment of the urinary sediment. At times they may possess a light yellow color. They are generally straight, rarely convoluted, and granular deposits are not frequently found in them.

*Granular Casts.*—Many regard these casts merely as hyaline material in which are embedded numerous granules. From the standpoint of accuracy, this is a mistake, as there is a difference between a granulated hyaline cast and a granular cast. The latter are short thick bodies, possessing a somewhat dark appearance and granules throughout. These granules consist of albumin (in rare

instances fat), and may be fine or coarse, giving rise to finely granular and coarsely granular casts. The granulated hyaline casts are longer, narrower and lighter. The granules are not as coarse and irregular transparent areas are apparent. These granules are composed of amorphous urinary salts (usually urates), which dissolve upon the addition of a drop of acetic acid.

*Epithelial Casts.*—Epithelial casts consist mainly of the epithelial cells lining the uriniferous tubules, and these casts are at times found covered with mineral and organic deposits. The individual cells are of varied shape and size, with a usually distinct nucleus. Epithelial casts are observed frequently in acute pathological conditions of the kidney.

*Fatty Casts.*—Under this heading are included casts in which the greater part of their surface area is covered with fat globules or crystals of fatty acids. They are met with usually in fatty degeneration of the kidneys.

*Blood Casts.*—Casts densely covered with erythrocytes constitute what is known as blood casts. The individual red blood cells may be of normal appearance, but more frequently they are decolorized and swollen. Occasionally other abnormal shapes are observed, representing various stages of degeneration. They are usually indicative of the occurrence of hemorrhage, which is not uncommon in acute renal disorders.

*Pigment Casts.*—In the later stage of renal hemorrhage, the blood cells in the cast are usually disintegrated. The breaking down of the erythrocytes leaves only flakes of pigment, which become imbedded within the cast, and form what is known as pigment casts.

*Leukocyte, Pus or Purulent Casts.*—In a chronic suppurative renal condition, which is not so frequently observed, these casts are met with. They are usually hyaline casts, thickly coated with masses of leukocytes, which may be of normal shape and size, or in a degenerative state. At times, they are mistaken for epithelial casts. Upon the addition of acetic acid, the neuclei become visible and the differentiation between these two types becomes easy.

*Fibrinous Casts.*—In cases of renal hemorrhage, there may be found casts composed almost entirely of coagulated fibrin. Upon the addition of acetic acid, they become almost invisible.

*Bacterial Casts.*—These are rare. They may be occasionally found in cases of suppurative nephritis. They differ from the true

casts, which are only occasionally covered with bacteria. These casts consist entirely of bacteria, usually the pyogenic cocci, closely packed together. They are differentiated from any granular debris, by their uniform shape and size, and also due to the fact that they are easily stained with aniline dyes.

*Calcareous Casts.*—There are few cases on record where true casts, exact moulds of the renal tubules, were observed in the urine of adults suffering with diseases leading to the formation of renal calculi. These were found to be either the phosphate or carbonate of calcium.

*Ammonium Urate Casts.*—Casts giving the reactions of ammonium urate have been met with in the urine of the new-born and other infants. According to many observers, their presence seems to have very little significance as a distinguishing feature in diseases.

*Spermatic Casts.*—These have been reported by some in cases of spermatorrhea. They are said to closely resemble hyaline casts, except that they are, as a rule, much longer and broader. The apparent absence of albumin is an important fact for differential diagnosis. No one has as yet established clearly the origin of these casts.

*Pseudo Casts* are bodies, of varied inorganic or organic origin, possessing somewhat a resemblance to true urinary casts, and may be mistaken at times by the inexperienced for true casts. Unlike the latter, these false casts have no definite relationship to renal disorders. Masses of urates, phosphates, oxalates, uric acid and other crystals, deposited on shreds of mucus, or crystallizing on other filamentous structures, produce forms, distantly resembling casts. The use of heat and appropriate microchemical reagents and practice will soon allow the inexperienced to avoid these as a source of error.

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## A NEW METHOD FOR THE ESTIMATION OF METHYL ALCOHOL.\*

BY S. B. SCHRYVER AND CYRIL CHRISTIAN WOOD.

A. ESTIMATION OF METHYL ALCOHOL IN WATER.—Some years ago, one of the authors described a method for the detection of formaldehyde, which could be applied to the quantitative estimation of very small amounts of this substance (*Proc. Roy. Soc.*, 1910, B. 82: 226,

\*From *The Analyst*, May, 1920.



and Reports of Inspector of Foods, Local Government Board, 1909, N. S. No. 12; also *Analyst*, 34: 470, 1909). The method in question consisted in treating the solution containing the formaldehyde with 1 per cent. solution of phenylhydrazine hydrochloride, then adding potassium ferricyanide, and afterwards concentrated hydrochloric acid, when, in the presence of the aldehyde, a brilliant fuchsine-like color was produced, which could be detected even when the concentration of formaldehyde did not exceed 1 in 2,000,000. This reaction forms the basis of the method for estimating methyl alcohol described in the present communication.

Several reagents are capable of oxidizing methyl alcohol to formaldehyde, but most of these interfere with the application of the test described above. This was not found, however, to be the case when ammonium persulphate was used. If an excess of the persulphate is added, the formaldehyde is oxidized further to carbon dioxide and water. By ascertaining the amount of persulphate that must be added to a given solution of methyl alcohol in water, so that after completion of the reactions under certain standard conditions of experiment formaldehyde just fails to be detectable by the above-mentioned reaction, the percentage of the alcohol present in the water can be estimated with a considerable degree of accuracy, even when the amounts present are as low as 0.0005 per cent.

When ammonium persulphate is heated with a solution of methyl alcohol three reactions can take place simultaneously, *viz.*, the decomposition of the persulphate itself, the oxidation of methyl alcohol to formaldehyde, and the oxidation of the aldehyde. It is, therefore, necessary to specify accurately the conditions under which the estimation should be carried out, as is the case in other oxidation methods, such as that of Fehling's, where several oxidation processes take place at the same time.

The method of carrying out the estimation is as follows: Samples, each of 5 Cc. of the methyl alcohol solution in water are introduced into a series of test-tubes (6 inches by  $\frac{3}{4}$  inch), and mixed with 5 Cc. of ammonium persulphate solution of varying concentrations. The test-tubes containing these mixtures are then inserted into a water bath containing boiling water, in which they are kept immersed for 10 minutes. At the end of this period 1 Cc. of the mixture is pipetted out from each tube and introduced into a series of smaller test-tubes, each of which contains 1 Cc. of 1 per cent. solution of phenyl-hy-

drazine hydrochloride; to these mixtures are then added 1 Cc. of a 2.5 per cent. solution of potassium ferricyanide and about 3 Cc. of concentrated hydrochloric acid. It will be found from this preliminary series of experiments that the concentration of methyl alcohol will lie between two limits—*viz.*, a higher limit corresponding to a concentration of the persulphate which is sufficient to oxidize completely the formaldehyde formed in the reaction, and a lower limit in which the concentration is insufficient, and the mixture of persulphate and methyl alcohol solution still gives a positive reaction for formaldehyde after heating for ten minutes. A second series of experiments can then be carried out in a similar manner to the first, mixing 5 Cc. of the methyl alcohol solution with 5 Cc. of persulphate in concentrations varying only between the two above-mentioned limits. The number of mixtures in this series can be varied according to the degree of accuracy which is desired in the estimations. If, for example, it was found that the mixture of 5 Cc. methyl alcohol solution mixed with 5 Cc. of 4 per cent. persulphate gave a negative reaction for formaldehyde in the first series of experiments, while the solution mixed with 5 Cc. of a 3 per cent. solution gave a positive reaction, in the second series of experiments the methyl alcohol solution was mixed with ammonium persulphate solutions varying only between 3 and 4 per cent. For each concentration of methyl alcohol, therefore, there corresponds a definite concentration of this persulphate which is just sufficient, under the specified conditions of experiment, to oxidize all the formaldehyde which is formed in the reaction.

TABLE I.

Per Cent. Persulphate in 5 Cc. Used for Oxidation.	Per Cent. of Solution of MeOH Used.	Cc. of This Solution in 10 Cc. Mixture.	Formaldehyde Reaction.	Concentration of MeOH in 5 Cc. Aqueous Solution.
5.0	1.0	1.45	+	0.29
5.0	1.0	1.40	o	0.28
4.0	0.5	2.4	+	0.24
4.0	0.5	2.3	o	0.23
3.0	0.25	3.45	+	0.1725
3.0	0.25	3.40	o	0.170
2.0	0.25	2.3	+	0.115
2.0	0.25	2.25	o	0.1125
1.0	0.1	2.8	+	0.056
1.0	0.1	2.7	o	0.054
0.5	0.1	1.5	+	0.030
0.5	0.1	1.4	o	0.028

0.25	0.05	1.5	+	0.015
0.25	0.05	1.4	o	0.014
0.10	0.025	1.0	+	0.0050
0.10	0.025	0.9	o	0.0045
0.05	0.010	1.3	+	0.0026
0.05	0.010	1.2	o	0.0024
0.025	0.005	1.3	+	0.0013
0.025	0.005	1.2	o	0.0012
0.010	0.001	2.5	+	0.00050
0.010	0.001	2.4	o	0.00048

In the above table are given the concentrations of methyl alcohol which are completely oxidized (so as to give a negative formaldehyde reaction) by concentrations of persulphate varying from 0.001 to 5 per cent.

The above table represents the final results of a detailed series of experiments, of which one is given *in extenso* to illustrate more clearly the method employed.

To determine the concentration of the solution of methyl alcohol which is just oxidized by a 5 per cent. persulphate solution, so that no formaldehyde is present after heating the mixture for ten minutes:

First Series:

Reaction  
(Formaldehyde).

5 Cc. of this 5 per cent. persulphate solution +		
5 Cc. of 1 per cent. solution of methyl alcohol	.....	strong pink
4 Cc. of 1 per cent. solution of methyl alcohol	1 Cc. H <sub>2</sub> O	pink
3 Cc. of 1 per cent. solution of methyl alcohol	2 Cc. H <sub>2</sub> O	pink
2 Cc. of 1 per cent. solution of methyl alcohol	3 Cc. H <sub>2</sub> O	pink
1 Cc. of 1 per cent. solution of methyl alcohol	4 Cc. H <sub>2</sub> O	o

Hence the concentration of methyl alcohol solution, 5 Cc. of which is completely oxidized by 5 per cent. persulphate, lies between  $\frac{1}{5}$  and  $\frac{2}{5}$  of one per cent.

To determine the concentration more accurately, the following second series of experiments was carried out:

Reaction  
(Formaldehyde).

5 Cc. persulphate solution +		
1.5 Cc. of 1 per cent. solution of methyl alcohol	3.5 Cc. H <sub>2</sub> O	faint pink
1.45 Cc. of 1 per cent. solution of methyl alcohol	3.55 Cc. H <sub>2</sub> O	just pink
1.4 Cc. of 1 per cent. solution of methyl alcohol	3.6 Cc. H <sub>2</sub> O	o
1.3 Cc. of 1 per cent. solution of methyl alcohol	3.7 Cc. H <sub>2</sub> O	o
1.2 Cc. of 1 per cent. solution of methyl alcohol	3.8 Cc. H <sub>2</sub> O	o
1.1 Cc. of 1 per cent. solution of methyl alcohol	3.9 Cc. H <sub>2</sub> O	o

Thus, if the end-point is taken to be that concentration which just gives the pink formaldehyde reaction after heating for ten minutes with the persulphate solution, it will be found that 5 per cent. of the latter just oxidizes 5 Cc. of a solution containing

$\frac{1.45}{5} \times 1 \text{ per cent.} = 0.29 \text{ per cent. methyl alcohol.}$  The percentages

of methyl alcohol corresponding to the various concentrations of persulphate are given in the final column of Table I. It is obvious that the concentration of a persulphate solution just necessary to oxidize a given concentration of methyl alcohol is a linear function of that concentration, and if  $c$  be the concentration (per cent.) of the persulphate,  $x$  that of the methyl alcohol, and  $k$  a constant, then  $x = kc$ . If this be calculated from the above table (neglecting the data for percentages of persulphate below 0.25 per cent.)  $k$  will be found to be  $= 0.059$ . These data were obtained with a methyl alcohol sample which had the correct boiling point, after careful fractionation over lime, and with a sample of persulphate in which the amount of ammonium persulphate was estimated by warming with a definite amount of standardized ferrous sulphate solution and determining the amount of the latter oxidized by titration against permanganate solution; this sample was found to contain 98.6 per cent. ammonium persulphate. In a series of experiments carried out with another sample of persulphate which was less pure, the constant  $k$  was found to be 0.054. In carrying out the estimation of methyl alcohol by the method above described, with any given sample of persulphate it is best to standardize 5, 4 or 3 per cent. solutions against methyl alcohol and to determine directly the constant  $k$ . Only a few experiments will be necessary, as the results will only differ slightly (by fractions of a Cc.) from the numbers given in Table I, column 3.

**B. ESTIMATION OF METHYL ALCOHOL IN ETHYL ALCOHOL.**—An attempt was made to estimate methyl alcohol in ethyl alcohol by the same method as that employed for estimating the methyl alcohol in water. This was found, however, to be impracticable, and there is no preferential oxidation of the lower alcohol by persulphate. It was found, for example, that the amounts of the latter necessary to oxidize to the end-point (disappearance of formaldehyde) did not differ, outside the limits of experimental error, with ethyl alcohol mixtures containing 4 and 5 per cent. of methyl alcohol. Another

method had therefore to be employed. This consisted in treating a persulphate solution with an excess of the mixture of alcohols, and examining the products produced in the initial stage of oxidation. It was then found that, under conditions such as these, the larger the amount of methyl alcohol present, the greater the amount of formaldehyde present, when the limited amount of persulphate used was entirely decomposed. The amount of formaldehyde produced under the conditions of the experiment could then be estimated colorimetrically. The estimations were carried out as follows: Ten Cc. of the ethyl alcohol containing methyl alcohol are diluted with 50 Cc. of water. Five Cc. of this are then mixed with 5 Cc. of a 1 per cent. solution of ammonium persulphate in a test-tube; this is provided with a short air condenser and heated in a boiling water bath for ten minutes. At the end of this period, 1 Cc. of the mixture is added to 1 Cc. of a 1 per cent. solution of phenyl hydrazine hydrochloride, *with which it is heated in a boiling water bath for five minutes*. After cooling, 1 Cc. of a 2.5 per cent. solution of potassium ferricyanide is added, and then 3 Cc. of concentrated hydrochloric acid. A pink color is thereby produced when methyl alcohol is present, which can be compared with the colors produced in a similar way from samples of ethyl alcohol containing known amounts of methyl alcohol. Experiments have been carried out with mixtures of ethyl alcohol and methyl alcohol, when the latter varied from 0.5 to 5 per cent., and it is possible by this rough comparison to estimate the percentage of methyl alcohol when contained within these limits to within 1 per cent. A more accurate estimation can be obtained when a colorimeter is employed. The method of carrying out the more accurate determination is described below.

It will be noticed, in the directions given above, that the reaction mixture is *heated* with the solution of phenylhydrazine hydrochloride before the other reagents are added, when carrying out the test for formaldehyde. The reason of this is that during the reaction certain quantities of the ethylal  $\text{HCH}(\text{OC}_2\text{H}_5)_2$ , and probably of the methylal  $\text{HCH}(\text{OCH}_3)_2$ , are formed during the heating, and the full pink color is not given by formaldehyde combined in these ways, unless the mixture is heated with the solution of phenyl hydrazine hydrochloride before adding the other reagents. (Compare Schryver, *Loc. cit.*)

In carrying out the more accurate colorimetric estimations, the pink test solutions prepared by the method described above were diluted with 70 Cc. of water, and the color was then compared with a

standard prepared in an exactly similar way from a sample of ethyl alcohol containing a known amount of methyl alcohol. When a colorimeter of Schmidt and Haensch was used, differences could be detected between samples of ethyl-methyl alcohol mixtures in which the amounts of methyl alcohol differed by only 0.2 per cent. Possibly, with a more modern form of colorimeter, more accurate estimations would be possible. The researches on the determination of the amounts of methyl alcohol in ethyl alcohol have, up to the present, been confined to mixtures containing between 0.5 and 5 per cent. of the former.

The sample of ethyl alcohol gave a faint formaldehyde reaction when oxidized, and the oxidation products were tested for methyl alcohol in the manner described above. Whether this is due to the fact that it contains small amounts of the lower alcohol, or to the fact that formaldehyde is formed in small amounts by the oxidation of ethyl alcohol, it is impossible at the present to say.

C. ESTIMATION OF METHYL ALCOHOL IN ACETONE.—It was found that a similar method could be applied to the estimation of methyl alcohol in acetone to that employed for estimating this alcohol in water, as the acetone is only oxidized to a slight extent by persulphate. In the former case, however, there were certain difficulties in carrying out the estimation, which have necessitated, when the percentage of methyl alcohol present is small, certain minor modifications in the process. It was found when the acetone contained 4 per cent. or more of methyl alcohol that, as a certain concentration of persulphate was exceeded, there was a sudden transition from the bright pink color yielded by the formaldehyde test to a light pink, and this latter color persisted even when the above-mentioned concentration of persulphate was considerably above this transition point. This phenomenon is probably due to the formation of a condensation product of formaldehyde with acetone, which is very resistant to oxidation by persulphate. When the amount of methyl alcohol in acetone falls below 4 per cent., the transition point is not very marked. At 4 per cent. and over, when higher concentrations of persulphate must be used, the point is unmistakable; for each given concentration of methyl alcohol in acetone, under the conditions of experiment described below, there corresponds a given concentration of persulphate, a small addition to which causes a sudden transition from a bright pink to a light pink, when the formaldehyde test is applied. By this method it is easy to determine

to within 0.2 per cent. the percentage of methyl alcohol in acetone when the former varies between 4 and 20 per cent. (above the latter limit no experiments were carried out). When the percentage is below the former limit it can be determined approximately by comparing the color reactions with those produced by acetone containing known amounts of methyl alcohol and when the experiments are carried out under the same conditions.

As an alternative method, when results accurate to within 0.2 per cent. can be obtained, the acetone mixture containing the lower percentage of methyl alcohol can be mixed with one containing a known higher percentage, so as to bring the total in the mixture to more than 4 per cent., and then carrying out the estimation of the methyl alcohol in this mixture by the method described in detail below, subsequently deducting the amount of added methyl alcohol from the result. A convenient method of carrying out the process is to add to the acetone-methyl alcohol mixture (containing the unknown amount of methyl alcohol) an equal volume of acetone containing 10 per cent. (by volume, as the specific gravities of methyl alcohol and acetone differ only very slightly) of methyl alcohol. By subtracting 5 from the percentage found in this mixture, and doubling the number thus obtained, the percentage of methyl alcohol in the mixture under investigation can be calculated.

The actual determination was carried out in the following manner: 5 Cc. of the acetone containing methyl alcohol under investigation were diluted to 250 Cc. with water. Quantities each of 5 Cc. of this mixture were introduced into a series of test-tubes ( $6'' \times \frac{3}{4}''$ ) containing 5 Cc. of ammonium persulphate solutions of varying concentrations.

TABLE II.

Per Cent. MeOH in Methyl Alcohol Acetone Mixture.	Formaldehyde Reaction after Heating with Persulphate Solutions of the Following Concentrations.				
	5 Per Cent.	4 Per Cent.	3 Per Cent.	2 Per Cent.	1 Per Cent.
10	o	?	+++	+++++	+++++
9	o	?	+++	+++++	+++++
8	o	o	+	+++	+++++
7	o	o	?	+++	+++++
6	o	o	o	++	+++++
5	o	o	o	+	+++++
4	o	o	o	?	+++
3	o	o	o	o	+++
2	o	o	o	o	+
1	o	o	o	o	?

The test-tubes were provided with corks containing short air-condensers, and were then introduced into a water bath containing boiling water in which they were kept immersed for ten minutes. At the end of this period each mixture was shaken, and the formaldehyde test was applied (using 1 Cc. of the hot solution) in the manner already given under the description of the determination of methyl alcohol in water. By using persulphate solutions of 1, 2, 3, 4, 5 per cent., an approximate estimation of the methyl alcohol can be made, as will be obvious from the table given above.

In the following table are given the percentages of persulphates in 5 Cc., which, when mixed with 5 Cc. of the diluted methyl alcohol acetone mixtures, just gave the positive reaction described above, which corresponds to the end-point.

TABLE III.

Per Cent. CH <sub>3</sub> OH in Original Mixture.	Per Cent. Concentration of Persulphate in 5 Cc. Added.	Per Cent. CHOH in Original Mixture.	Per Cent. Concentration of Persulphate in 5 Cc. Added.
20.0	6.4	8	2.56
17.5	5.8	7	2.24
15.0	4.8	6	2.04
12.5	4.0	5	1.7
10.0	3.2	4	1.45
9.0	2.9	..	....

The above researches were carried out for the Food Investigation Board.

CONCLUSIONS.—(1) A method for estimation of methyl alcohol in water is described, the essential principle of which consists in determining the concentration of ammonium persulphate necessary to destroy completely the formaldehyde formed in the initial stages of the oxidation process under certain specified conditions of experiment. For the detection of formaldehyde the method previously described by one of the authors has been employed.

(2) By a slight modification of this method the amount of methyl alcohol in acetone can be estimated.

(3) To determine the amount of methyl alcohol in ethyl alcohol, the mixture of alcohols is partially oxidized by a relatively small amount of persulphate (the alcohols being in excess), and the formaldehyde formed under these conditions is estimated colorimetrically.



## THE NATURE OF THE FAT-SOLUBLE VITAMIN\*

The discovery of the dietary importance of that property of many foods which is now termed fat-soluble vitamin or fat-soluble A represents a contribution of American physiologists<sup>1</sup> to the science of nutrition. It has been repeatedly verified both in this country and abroad. According to the observations made on a variety of experimental animals, the lack of the fat-soluble vitamin in the diet during adolescence may lead to an inhibition of growth together with symptoms of decline in health. Most conspicuous in a specific way is the apparently increased susceptibility to bacterial infection. In the case of rats this lowered resistance first betrays itself in many instances by the appearance of a characteristic disorder of the external eye which has provisionally been classed as a xerophthalmia. It usually begins with a swelling of the lids which is followed by an inflamed and catarrhal condition of the conjunctiva. This rapidly becomes worse, and the discharge, which is at first hemorrhagic, frequently becomes purulent. If untreated, the cornea may become involved and total blindness result. If a food containing fat-soluble vitamin is administered, the symptoms usually clear up in a few days without further treatment, and growth is resumed. The same phenomena have been observed in mice, and more recently in rabbits kept on diets poor in the fat-soluble vitamin.<sup>2</sup> A possible relation of the lack of the latter to the occurrence of phosphatic calculi has also been pointed out by Osborne and Mendel.<sup>3</sup>

Whether and in what manner a dietary deficiency in fat-soluble vitamin plays a part in human disease remains to be ascertained. The probability of the need of this food accessory in the ration of man is large and the possible dire effects of a lack of it are being discussed widely at present, notably in relation to the pathogenesis of pellagra, rickets and xerophthalmia in childhood. The fact that many fats, such as lard, vegetable oils and hydrogenated fats, which have found widespread use in the dietary of man in recent years, are

\* From the *Jour. Amer. Med. Assoc.*, Aug. 21, 1920.

<sup>1</sup> McCollum, E. V., and Davis, M.: *J. Biol. Chem.*, 15: 167, 1913; Osborne, T. B., and Mendel, L. B., *Ibid.*, p. 311.

<sup>2</sup> Nelson, V. E., and Lamb, A. R.: "The Effect of Vitamine Deficiency on Various Species of Animals, I. The Production of Xerophthalmia in the Rabbit," *Am. J. Physiol.*, 51: 530 (Apr.), 1920.

<sup>3</sup> Osborne, T. B., and Mendel, L. B.: "The Incidence of Phosphatic Urinary Calculi in Rats Fed on Experimental Rations," *J. A. M. A.*, 69: 32 (July 7), 1917.

virtually devoid of fat-soluble vitamin has caused some concern owing to the relatively high cost of those fats, like milk fat and egg fat, which are rich in it. It is a relief to know, however, that the fat-soluble vitamin has a far wider distribution in nature than the earlier studies led physiologists to suspect. Only recently the researches of McCollum, Steenbock and their collaborators at the University of Wisconsin,<sup>1</sup> and of Osborne and Mendel<sup>2</sup> in New Haven, have indicated the richness of many sorts of plant tissues in all familiar types of vitamins, thus placing the dietary importance of "vegetables" in a new light.

In commenting on this information, Osborne and Mendel remark that it emphasizes the use of vegetables to supplement the refined foods of the modern food industry which furnishes products rich in proteins, fats and carbohydrates, but in many cases comparatively deficient in the vitamins. The newly acquired facts, they add, serve as a further reminder that the fat-soluble vitamin need not be sought solely in foods known to be rich in fats. Fat-soluble vitamin has never been isolated, nor has it been concentrated in any way which avoids the simultaneous presence of ordinary fats, to some extent at least. Although its reactions and behavior toward solvents suggest a lipoidal character, Steenbock and Boutwell<sup>3</sup> have demonstrated that the fat-soluble vitamin resists saponification with alkalis whereby true fats are converted into soaps. Hence it can scarcely be regarded as identical with fats. This fact, for which some evidence had already been available, represents a distinct step in advance in the study of vitamins.

The extracts containing fat-soluble vitamin as obtained from natural products are invariably colored. Yellow corn is richer in fat-soluble vitamin than is white corn; there is a similar contrast be-

<sup>1</sup> Steenbock, H., and Gross, E. G.: "Fat-Soluble Vitamine, II. The Fat-Soluble Content of Roots, together with Some Observations on Their Water-Soluble Vitamine Content," *J. Biol. Chem.*, 40: 501 (Dec.), 1919; "IV. The Fat-Soluble Vitamine Content of Green Plant Tissues, together with Some Observations on Their Water-Soluble Vitamine Content," *Ibid.*, 41: 149 (Feb.), 1920; McCollum, E. V.: "Newer Knowledge of Nutrition," New York, 1919.

<sup>2</sup> Osborne, T. B., and Mendel, L. B.: "The Vitamines in Green Foods," *J. Biol. Chem.*, 37: 187 (Jan.), 1919; "Nutritive Factors in Plant Tissues, IV. Fat-Soluble Vitamine," *Ibid.*, 41: 549 (Apr.), 1920.

<sup>3</sup> Steenbock, H., and Boutwell, P. W.: "Fat-Soluble Vitamine, VI. The Extractability of the Fat-Soluble Vitamine from Carrots, Alfalfa, and Yellow Corn by Fat Solvents," *J. Biol. Chem.*, 42: 131 (May), 1920.

tween colorless lard and the yellow milk fat and egg fat. Hence Steenbock<sup>1</sup> has advanced the theory that the vitamin may be yellow pigment or at any rate a closely associated substance. His latest contribution is corroboratory; it also indicates that the vitamin attends the carotin rather than the xanthophyll variety of pigments, either or both of which may represent the yellow coloring matter in animal and plant foods. These findings, if they are further substantiated, mark a distinct step in advance toward the goal of discovering the nature of the fat-soluble vitamin.

### SOME RECENT SAMPLES OF "GREY" CINCHONA BARK.\*

BY BERNARD F. HOWARD, F.I.C., AND OLIVER CHICK, A.I.C.

Grey Bark of Huanuco (a locality of Lower Peru) was a fairly common kind of Peruvian bark to be met with on the London market in the sixties and seventies, but, owing to its low quinine content and the severe competition of rich Java barks, its importation gradually diminished, and for the last twenty years, at any rate, it has been almost unknown as a bark of commerce.

The temporary shortage of cinchona due to the war, however, has caused it to reappear, and the authors have had the opportunity of studying several samples of good-sized parcels from the point of view of modern analytical methods.

The literature of Grey Bark dates almost entirely from the period mentioned above, botanically. Weddell, in his "Notes on the Quinquinas," published in 1871, p. 39, states that *Cinchona nitida* together with *C. Peruviana* and *C. micrantha*, supplies the market with "Quinquina gris," or grey bark, and it seems generally agreed among all experts that a normal sample of grey bark would be expected to contain these three varieties.

From the analytical point of view, most of the published work, dating back some fifty years or more, is necessarily vague, owing probably to the fact that the methods of separation and estimation of the various alkaloids in the bark were at that time very uncertain. J. E. Howard stated (Pereira, "Mat. Med.," Vol. II, Pt. II, p. 98, fourth edition) that he found "nearly twice as much

<sup>1</sup> Steenbock, H.: "White Corn vs. Yellow Corn and a Probable Relation between the Fat-Soluble Vitamine and Yellow Plant Pigments," *Science*, 50: 352 (Oct. 10), 1919.

\*Reprinted from *The Pharmaceutical Journal and Pharmacist*, July 24, 1920.

cinchonine as quinine," and Delondre and Bouchard found cinchonine in relation to quinine sulphate in the proportion of 4 to 1.

From some old records of J. E. Howard it would appear that on analysis a typical grey bark of that period would yield about 0.45 per cent. quinine sulphate and about 0.90 per cent. cinchonine alkaloid. A parcel of thirty-eight bales, mark "D. F. C.," ex. s.s. "Cedric," was analyzed early this year, and the authors obtained the following results, which are fairly well in keeping with the references given above:

Quinine Alkaloid.....	0.45 per cent.
Cinchonidine Alkaloid.....	0.22 "
Cinchonine Alkaloid.....	0.63 "
Quinidine Alkaloid.....	nil
Amorphous Alkaloid.....	0.48 "
<hr/>	
Total Alkaloid.....	1.78 "

The selling analysis quoted by the merchant showed quinine 0.42 per cent., and total alkaloid 1.49 per cent., which closely agrees with the authors' fuller separation of the alkaloids given above.

Another parcel of "Loxa" bark recently analyzed, apparently of the same type, contained quinine alkaloid 0.33 per cent. and cinchonine alkaloid 0.58 per cent.

These two recent parcels appear to conform to the old standards of typical grey bark, and call for no special comment, but the following large parcel, the details of which are given below, is, in the authors' opinions, unique in the history of the Cinchonaceae.

In March, 1920, we received from the same source a sample of a parcel of 138 bales of South American cinchona bark (marked "D F. C.," ex. s.s. "Elder Branch"), together with an analytical report that it contained 6 per cent. of alkaloids, but only minute traces of quinine. The sample was therefore submitted to a very thorough examination, with most surprising results, which fully bore out the analyst's statement above mentioned:

Quinine Alkaloid.....	0.027 per cent.
Cinchonine Alkaloid.....	5.490 "
Amorphous Alkaloid.....	0.785 "
<hr/>	
Total Alkaloid.....	6.302 "

There were evidences of very small quantities of quinidine, but apparently no cinchonidine was present.

In order to confirm the cinchonine value, the separated alkaloid was examined by the optical test, and gave exactly the correct value for  $\alpha$ .

The bark was then submitted to Mr. E. M. Holmes for his opinion, and was reported as Grey Bark of Huanuco. The bulk of the sample consisted of *Cinchona nitida* (Pereira, "Mat. Med.," Vol. II, Pt. II, p. 98, fourth edition) and *Cinchona Peruviana* (J. E. Howard), together with a small amount of *Cinchona officinalis*. As mentioned above, grey bark as known on the market in the sixties and seventies usually contained the first two varieties, together with *Cinchona micrantha*, which was absent in the sample under examination. There would seem to have been some doubt in the past as to whether or not the *Peruviana* of J. E. Howard was identical with *Cinchona nitida* of Ruiz and Planchon, and in order possibly to throw some light on this point the first two varieties, as sorted out of the bulk sample by Mr. Holmes, were again examined analytically:

<i>Cinchona Nitida.</i>	Per Cent.	<i>Cinchona Peruviana,</i> Per Cent.
Quinine Alkaloid.....	} 0.20	0.28
Cinchonidine Alkaloid.....		
*Cinchonine Alkaloid.....	5.08	5.04
Quinidine Alkaloid.....	Trace	Trace
Amorphous Alkaloid.....	0.82	1.28
<hr/>		<hr/>
Total Alkaloid.....	6.10	6.60

\*The cinchonine was again checked by optical test, and gave a specific rotation of  $208^{\circ}$  and  $212^{\circ}$ , respectively, which is sufficiently close to Allen's figure of  $226^{\circ}$  for identification purposes.

The average of two tests (6.35 per cent.) confirms the first result of the samples as a whole (6.302 per cent.).

From the analytical point of view, therefore, the alkaloidal contents of the *Peruviana* was practically identical with the *Nitida*.

It therefore remained to compare the two barks, microscopically, and Mr. Holmes kindly undertook to have this examination carried out.

The authors feel that they cannot do better than give this report in full:

The microscopic examination of the bark indicates that it is in all probability a form of *Cinchona Peruviana*, Howard, remarkably rich in cinchonine, bearing somewhat the same relation to that species that *Cinchona Ledgeriana* does to *Cinchona Calisaya* Wedd.

The bark from which the sample was taken is evidently the bark recognized in commerce as Huanuco or Lima bark. This bark is stated by Pereira to be collected in Cuchero and Huanuco and exported from the Peruvian port of Lima (Callao). In his time, about 1857, two distinct barks were found to be mixed under this name, one referred to *Cinchona nitida* R. and P., and the other to *C. micrantha* Wedd., the *C. nitida* being distinguished as "fine grey bark" and the *C. micrantha* as "inferior or coarse grey bark" and (Pereira, "Mat. Med.," 4th Ed., 1857, Vol. II, Pt. II, p. 98, 99), but both of these barks were then imperfectly known. But the various species sent into commerce under the name of grey or Huanuco bark appear to have changed in course of time, for Vogl, "Pharmacognosie," p. 286, states that Huanuco bark was then (1896) derived from *C. macrocalyx*, mixed with a large proportion of the barks of *C. ovata* and *C. Peruviana*, but rarely with that of *C. micrantha*.

Planchon, "Drogues Simples," Vol. II, p. 124 (1896), states that the Huanuco bark was usually derived from three distinct species, viz., *Cinchona nitida* R. and P., *C. micrantha* R. and P., and *C. Peruviana* How., the first named being then very rare, and *C. Peruviana* constituting the principal portion of Huanuco bark. Fortunately, he gave two illustrations of the microscopic structure of *C. nitida* and *C. Peruviana* How., that of *C. nitida* agreeing fairly well with the illustration of that bark in Berg's "Anatomischer Atlas," published in 1865. taf. 34, No. 80, where an illustration of *C. micrantha* is also given on the same page, No. 82. Berg, however, expressly states that the *C. nitida* he illustrates is not that described by J. E. Howard, but is the *C. nitida* of Ruiz and Pavon, is the *Cascarilla Peruviana* of Pavon. Like that of Planchon, the illustration indicates the absence of laticiferous vessels and stone cells in the cortical parenchyma, while they are abundantly present in Planchon's *C. Peruviana*. This species, however, is not given in Berg's atlas. These two features are also absent from the illustration of *C. micrantha* given by Berg.

The specimen of Huanuco bark recently received from B. F. Howard is seen under the microscope to consist chiefly of bark belonging to the group in which laticiferous cells and sclerenchymatous cells are distributed through the cortical parenchyma. This group includes *Cinchona ovata*, *C. Pelleteriana*, *C. Peruviana*, *C. purpurea* and *C. umbellifera*. The bark in question must therefore

belong to one of these species or to an undescribed species belonging to the same group.

Of those Cinchonas to which Huanuco bark has been attributed by different authorities, *C. micrantha* and *C. nitida* are excluded by reason of containing neither laticiferous vessels nor sclerenchymatous cells in the cortical parenchyma; also *C. macrocalyx* because although it shows sclerenchymatous cells it has no laticiferous vessels. The choice of known species rests, therefore, between those of the group just mentioned. Of these, *C. umbellifera* is characterized by having very few sclerenchymatous cells and a resinous zone under the periderm, and very small bast cells, somewhat regularly but radially arranged in narrow lines, and the cells of the medullary rays are represented as broader than long. According to Berg, this species is found abundantly in Huanuco bark.

In *C. ovata* the cork consists of colorless, not brown, cells. This bark may be, therefore, left out of consideration, as in Mr. B. F. Howard's bark they are dark brown.

*C. Pelleteriana* has liber cells varying much in diameter, and also shows club-shaped liber cells (stabformig) in the bark, and it is not known to occur in Huanuco bark.

*C. purpurea* has also a pale cork like *C. ovata*. Like *C. Pelleteriana*, it contains club-shaped liber cells. It is sometimes found in Huanuco bark, but the pale cork distinguishes it from the bark under consideration.

*C. Peruviana* is not described by Berg, but is described by Vogl, *Loc. cit.*, p. 287, 288, and also by Planchon, who gives an illustration of it (*Loc. cit.*, p. 125). It is characterized by Vogl as having numerous club-shaped liber cells and crystal cells and the laticiferous cells often filled with thyllae. The laticiferous vessels form a single or double ring. The external appearance of this bark is described by Vogl as of a prevailing grey-brown color with yellowish, greenish, and whitish patches, with distant transverse cracks and well marked long fissures, and is of a cinnamon-brown color on the inner surface.

Planchon and Collin, *Loc. cit.*, p. 124, state that the small quills of *C. Peruviana* have a finely cracked periderm of a grey or slightly bluish tint and closely adherent to the liber, the transverse cracks being few and shallow. The larger quills always present a more or less dark grey tint and are characterized by the presence of white patches and longitudinal depressions, which are more or less clearly

marked. The transverse cracks often extend nearly round the large quills. The microscope shows a thick layer of cork cells, isolated sclerenchymatous cells in the cortical parenchyma, and the liber fibers are mostly isolated and arranged in radial lines.

The specimens received from Mr. B. F. Howard consist mainly of pieces of bark exhibiting the characters attributed to *C. Peruviana* How., by Planchon and Collin, and show the anatomical structure of that bark as illustrated and described by those authors and also as described by Vogl. Some of the pieces differ in the greater number of sand cells and in the smaller number of the stone cells in the cortical parenchyma.

The larger percentage of cinchonine found in this shipment of Huanuco bark may possibly be due to the elevation at which the trees grow, as this factor and the accompanying differences of heat and moisture are known to influence the character of the alkaloids present. In the present state of our knowledge of the species of the *Cinchona* genus occurring in Peru I can only come to the conclusion that the bark submitted to me for examination is the produce of one, or possibly more, forms of *C. Peruviana* How., as interpreted in the illustration given by Planchon and Collin and Berg.

The authors were at a loss to understand the presence of *Cinchona officinalis* in a grey bark, and they also considered that if this variety were present in any quantity it would inevitably affect the alkaloidal contents. As has been shown above, *nitida*, *Peruviana*, and *micrantha* have always appeared to yield an exceptionally large amount of cinchonine, and this peculiarity has never been known to occur in the much less rare *officinalis* bark.

In order to establish the presence or otherwise of "*officinalis*" in this parcel, a fresh sample was drawn from the bulk, and again submitted to Mr. Holmes for his opinion. In this fresh sample he could find no *C. officinalis*, but classified it into three varieties. *nitida*, *Peruviana*, *micrantha*, together with another variety somewhat resembling *Pitayensis*, and which might either belong to this or the *Lucumaeifolia* variety, or might possibly be a new variety altogether. From this examination it is fair to assume that the presence of a small quantity of *officinalis* in the first sample was purely accidental and not typical of the parcel, and that the amount was so small that it did not affect the unusual distribution of alkaloids.

The analyses of the varieties, as identified by Mr. Holmes, were as follows:



	<i>C. Micrantha.</i> Per Cent.	<i>C. Nitida.</i> Per Cent.	<i>C. Peruviana.</i> Per Cent.
Quinine Alkaloid } .....	0.08	0.05	0.11
Cinchonidine " } .....			
Cinchonine " .....	4.49	5.64	5.12
Quinidine " .....	trace	trace	trace
Amorphous " .....	0.33	0.30	0.50
Total Alkaloid .....	4.90	5.99	5.73

The amount of the obscure variety resembling *Pitayensis* was not sufficiently large to warrant a separate analysis, and it was considered important to preserve it intact as a specimen for future reference.

Mr. Holmes has expressed the opinion with regard to this exceptional parcel of grey bark that the abnormally high proportion of cinchonine indicates growth at a low elevation and a hot, moist atmosphere, basing his assumption on a statement by J. E. Howard (*Pharm. Journal*, 1883, XIII, p. 1013), that under these circumstances cinchonine is increased and quinine decreased.

Mr. Holmes also compares the contents of this sample with the well-known *Ledgeriana* variety of *Cinchona Calisaya*, in which quinine alone is present up to a high percentage (the present authors have analyzed samples of this bark containing up to 12 per cent. of quinine, expressed as sulphate) and the other alkaloids only in very small proportions. He also puts forward the extremely interesting supposition that if, under peculiar circumstances of cultivation, a variety of *Calisaya* bark can be produced with such a large proportion of quinine, so in the case of *Cinchona Peruviana* or *C. nitida* it is equally possible that under favorable conditions a variety should be found in which the high cinchonine value peculiar to this species is exaggerated almost to the point of extinction of the other alkaloids.

If this interesting supposition is accepted it goes far to account for the peculiar contents of the samples under discussion which at first sight seems almost inexplicable.

For many years past the commercial value of bark for manufacturing purposes (as distinct from druggists' bark) has been based almost entirely on the percentage of quinine present, but quite recently the great stimulation of interest in the hydrogenated derivatives of the various natural alkaloids has caused the distribution of the other principal bases, such as cinchonidine, cinchonine,

and quinidine in the bark, to be a matter of some importance and consequently any information regarding the conditions under which Nature herself tends to "separate" particular alkaloids in various species of Cinchona may be of considerable commercial value in the future, and not merely a question of academic interest.

The authors have made free use of the very valuable report and suggestions of Mr. Holmes, and it is partly at his request that this note is brought before the Conference.

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### THE SPREAD OF NOXIOUS PLANTS.\*

Considerable consternation has been caused in the neighborhood of Wagga (N. S. W.) by the discovery that St. John's Wort has taken a firm hold of certain parts of the district, and threatens to render valueless a considerable tract of country if its spreading cannot be prevented. There are several parts of the commonwealth in which this pest has taken such a hold that cultivation has become a difficulty, and the native herbage has been destroyed by the invader.

The *Hypericum perforatum* has long been esteemed in medicine, and was formerly official in the French Codex. It is still esteemed among herbalists in the United States as a stimulating expectorant and emmenagogue, and a diuretic, as well as a local application for local pains, contusions, and burns. It is said to have been first introduced into Victoria by a German woman who practiced as a herbalist, and who cultivated it for medicinal purposes. It has spread to an alarming extent, and the Pastures Protection Board of the Wagga district are taking vigorous steps for its eradication, and to prevent it spreading to district lands. The weed was discovered growing by the roadsides and in vacant blocks of land, and the town council have been urged to take immediate steps to prevent its further spread.

Mr. J. H. Maiden, F.R.S., Director of the Sydney Botanic Gardens, recently offered to supply persons desirous of obtaining the seeds of the red poppy gathered in the Somme valley battlefields, and from the school children of Villers-Brettonneux with small quantities of this seed for garden cultivation, to remind them of the brave soldiers who fell there. This was met with a vigorous protest and the statement was made through the columns of the daily press that we have quite enough noxious plants and animals in New South

\* From the *Australasian Journal of Pharmacy*.

Wales without adding to the number the French red poppy, which, like the Scotch thistle, may first be cultivated as a garden plant, but on being allowed to spread may prove difficult of eradication. The lantana or Cape stink weed is an evidence of the danger that may arise from the introduction of a flowering plant into a climate and country particularly suitable for its propagation. The foxglove has become a noxious weed in New Zealand, and among the tobacco crops of New England there has been a difficulty in eradicating the henbane. Sweet fennel is classed among the noxious plants by the Department of Agriculture of this state, and its cultivation is prohibited.

Mr. C. G. Orr, pharmacist, of Port Macquarie, has been experimenting in growing several tropical plants, and is said to have met with considerable success in the cultivation of the Cavendish banana and the pineapple. Mr. George Turvey is another pharmacist who has been studying the cultivation of medicinal plants on his allotment at French's Forest. The work of Mr. Orr has been favorably commented upon by the agricultural editors of the daily press.

F. W.

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### THE PURIFICATION OF CRUDE COCAINE.\*

The separation of the various bases obtained during the process of extracting coca leaves with sodium carbonate and petroleum ether has been made the subject of an exhaustive study by Dr. L. R. de Rosemont, of the University of Geneva (*Jour. Suisse de Pharm.*, April 29, 1920). He first established the solubility of the various bases in different solvents, and found that cocaine, cinnamyl-cocaine, isococaine, and isotropyl-cocaine were all easily soluble in ether, alcohol, chloroform, ligroin, and benzene. Crude cocaine is partly soluble in water, and contains about 10 to 13 per cent. of sodium carbonate and bicarbonate, in addition to chlorides and alkaline sulphates.

Dr. de Rosemont describes twelve different methods he investigated for obtaining pure cocaine, including a study of the processes described in four German patents. The process he considers best (it yields from 79 to 81 per cent. of chemically pure cocaine) is as follows: Ten grams of crude cocaine is dissolved in hot water containing 5 grams of  $\beta$ -naphthalene-sulphonic acid, and the solution

\* From *The Chemist and Druggist*, July 3, 1920.

is filtered while warm. On cooling it deposits an oily-resinous body which soon becomes a semi-crystalline mass. Ammonium carbonate is added until the solution becomes cloudy, then solution of ammonia, which produces a beautiful white precipitate. This is extracted with ether and the pure cocaine crystallizes out from the ethereal solution. The  $\beta$ -naphthalene-sulphonic acid may also be recovered by concentrating the mother liquors and precipitating with hydrochloric acid.

Another process recommended by the author consists in dissolving 10 grams of crude cocaine in boiling water containing acetic acid. On cooling, the solution is precipitated by the addition of ammonium carbonate, which yields a resinous, yellowish precipitate, lighter than water. The solution is filtered and solution of ammonia added in excess, the almost chemically pure cocaine which is precipitated is extracted with ether, from which it crystallizes spontaneously. This method also yields 79 to 81 per cent. of chemically pure cocaine. In addition to separating the cocaine from the crude product, the author also dealt with the question of utilizing the residue (*i. e.*, the resinous precipitate first thrown down) obtained in the course of precipitating the pure alkaloid, particularly the possibility of transforming the ecgonine present in this residue into cocaine. This residue is purified by crystallization from alcohol, and pure ecgonine is precipitated afterwards by means of carbonate of sodium. The pure ecgonine thus obtained is then dissolved in methyl alcohol, and the solution treated with anhydrous hydrochloric acid, yielding methyl-ecgonine hydrochloride; the unaltered ecgonine is then extracted with ether. Of the methyl-ecgonine thus obtained, 20 grams is heated on a water bath with benzoyl chloride 20 grams, until no more hydrochloric acid is evolved. The solution is now added to cold water, whereby benzoic acid is precipitated; this is filtered out and the filtrate concentrated. The synthetic cocaine (termed coca-ethyline in the German patent 47,713) is then precipitated from the filtrate by the addition of solution of ammonia. By this method of treating the residue a further yield of 5 to 10 per cent. of cocaine is obtainable.

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## RAT POISONS.\*

Phosphorus, arsenic, and strychnine, says Mr. Thomas Parker, F.R.C.V.S., in a paper published in *The Veterinary Journal*, are often used in the preparation of rat-pastes or vermin killers, but, as they are all rapidly fatal in their effects on man and the domestic animals, and therefore dangerous, are not recommended. There are others which, while being rapidly fatal to rats, are comparatively harmless to domestic animals. These are barium carbonate and squill.

*Barium Carbonate.*—Although  $1\frac{1}{2}$  to 2 grains suffices to kill a rat, barium carbonate is more or less harmless to domestic animals, cats and chickens withstanding 10 to 15 grains, and an average-sized dog over 100 grains. It has also the advantage of being cheap, tasteless, odorless, and therefore easily made attractive by mixing with a suitable bait, and has been found to be as effective as the more dangerous poisons, such as phosphorus and arsenic. The bait may be prepared in the following manner: Make a paste by well mixing equal parts of the powdered barium carbonate and tallow-fat or dripping, and spread it over thin slices of bread exactly as one would do with butter. Then, having firmly pressed the slices together to form sandwiches, they are cut into small squares ready for use. Of course, it may be mixed with any other bait found equally or more acceptable. Owing to the action of barium carbonate on the lining membrane of the stomach the rats are induced to leave their holes in search of drink. It is recommended, therefore, to place within reach on the day following the treatment, shallow bowls containing a solution consisting of equal parts of liquid squill and milk, the rats being thus made to partake of more poison in their efforts at relief.

Squill may be obtained either in the form of a powder or of a solution. Although comparatively harmless to domestic animals, it is extremely toxic as far as rats are concerned, the minimum lethal dose being only half a grain. Mix the powdered squill with tallow or dripping, or with either of these fats and oatmeal. The mixture should be smeared on bread, the latter being then cut into small pieces. In the liquid form squill may be prepared for use in the following manner: Mix equal parts of liquid squill and milk, and to each pint of the solution add 1 lb. by weight of bread.

Of all rat poisons squill solution is believed to be the most effective, and has been recommended in preference to barium carbonate for the following reasons:

\* From *The Australasian Jour. of Pharm.*, June 21, 1920.

(a) It is three times as toxic for rodents.

(b) It is even less harmful to most domestic animals.

The one point against the use of squill, however, lies in the fact that at present it is somewhat more expensive than most other poisons.

There is always a possibility of a rat dying under flooring or behind wainscoting, either through poison or otherwise. If a rat from a drain takes poison and cannot regain its habitation, the carcass will most probably become putrid. If such a rat dies near a fireplace or hot-water pipe, the stench will be intensified. Chloride of zinc is a good deodorizer in such cases, and combines with and neutralizes the offensive chemical products of putrefaction. If necessary, a hole should be bored with a bit and brace in the vicinity of the supposed source of origin of the odor if possible. Some perfume or pinewood oil can be added to the zinc chloride, which should be applied through the hole. A cork will close the orifice, and can be withdrawn from time to time to ascertain whether the nuisance has abated. Where possible, however, it is advisable to remove the carcass immediately its presence has been detected.

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### THE CHEMISTRY OF ODORS.\*

Man and animals alike depend on their senses not only for physiologic delight but also for the warnings against various dangers of their environment. The "twin senses" smell and taste exercise a peculiarly valuable function in that they stand "like sentries at the portals of the body, where they closely scrutinize everything that enters." Slosson<sup>1</sup> has fancifully remarked that these two special senses lead us to the heart of the molecule and enable us to tell how atoms are put together. Sounds and sights may be disagreeable, but they are never fatal. A man can live, Slosson writes, in a boiler factory or in a cubist art gallery, but he cannot live in a room containing hydrogen sulphide. Until recently there has been little dependable information available about the chemical nature of the odoriferous substances encountered in daily life. The so-called essential oils, many of which have a "fruity" odor, have been prepared for some time in the laboratory. Experts remind us, however, that the artificial fruit essences are usually composed of a mixture of substances without any guarantee of their actual occurrence in the fruits whose

\* From *Jour. Amer. Med. Assoc.*, Aug. 14, 1920.

<sup>1</sup> Slosson, E. E.: "Creative Chemistry," New York, The Century Company, 1920.

flavors they are supposed to represent. An actual identification of the principal flavoring constituent of an edible fruit was apparently first accomplished in 1913 by Kleber,<sup>1</sup> who showed by accurate methods that ripe bananas actually contain amyl acetate, the substance commonly designated as "pear oil." Recently Power and Chestnut<sup>2</sup> of the Bureau of Chemistry in the U. S. Department of Agriculture at Washington have unraveled some of the mysteries of the apple. They obtained no evidence that amyl valerate, familiarly designated as "apple oil," is present in the fruit. Its odorous constituents were found to consist essentially of the amyl esters of formic, acetic and caproic acids, with a very small amount of the caprylic ester and a considerable proportion of acetaldehyde. It is not unlikely that some of the alcohol and acids mentioned are also present in the free state. All of these various substances occur in mixtures of varying proportions in the numerous varieties of the apple, thus giving rise to slight differences of odor. The quantities actually present, for example, 0.0007 per cent. in the Ben Davis and 0.0013 per cent. of essential oil in the more odorous crab-apple, may seem small. Nowadays, however, the physician who deals with antigens and antitoxins, with radium, with vaccines and vitamins, has become accustomed to the possible potency of products in small quantities.

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INTERNATIONAL ATOMIC WEIGHTS, 1921.\*

The report of the International Committee on Atomic Weights is given in the following table:

Symbol.	Atomic Weight.	Symbol.	Atomic Weight.
Aluminum.....Al	27.1	Calcium.....Ca	40.00
Antimony.....Sb	120.2	Carbon.....C	12.005
Argon.....A	39.9	Cerium.....Ce	140.25
Arsenic.....As	74.96	Cesium.....Cs	132.81
Barium.....Ba	137.37	Chlorine.....Cl	35.46
Bismuth.....Bi	208.0	Chromium.....Cr	52.0
Boron.....B	10.9	Cobalt.....Co	58.97
Bromine.....Br	79.92	Columbium.....Cb	93.1
Cadmium.....Cd	112.47	Copper.....Cu	63.57

<sup>1</sup> Kleber, C., *Am. Perfumer*, 7: 235, 1913.

<sup>2</sup> Power, F. B., and Chestnut, V. K.: "The Odorous Constituents of Apples; Emanation of Acetaldehyde from the Ripe Fruit," *J. Am. Chem. Soc.*, 42: 1509 (July), 1920.

\* *Journal Amer. Chem. Soc.*, Sept.

	Symbol.	Atomic Weight.		Symbol.	Atomic Weight.
Dysprosium.....	Dy	162.5	Phosphorus.....	P	31.04
Erbium.....	Er	167.7	Platinum.....	Pt	195.2
Europium.....	Eu	152.0	Potassium.....	K	39.10
Fluorine.....	F	19.0	Praseodymium.....	Pr	140.9
Gadolinium.....	Gd	157.3	Radium.....	Ra	226.0
Gallium.....	Ga	70.1	Rhodium.....	Rh	102.9
Germanium.....	Ge	72.5	Rubidium.....	Rb	85.45
Glucinum.....	Gl	9.1	Ruthenium.....	Ru	101.7
Gold.....	Au	197.2	Samarium.....	Sa	150.4
Helium.....	He	4.00	Scandium.....	Sc	45.1
Holmium.....	Ho	163.5	Selenium.....	Se	79.2
Hydrogen.....	H	1.008	Silicon.....	Si	28.3
Indium.....	In	114.8	Silver.....	Ag	107.88
Iodine.....	I	126.92	Sodium.....	Na	23.00
Iridium.....	Ir	193.1	Strontium.....	Sr	87.63
Iron.....	Fe	55.84	Sulphur.....	S	32.06
Krypton.....	Kr	82.92	Tantalum.....	Ta	181.5
Lanthanum.....	La	139.0	Tellurium.....	Te	127.5
Lead.....	Pb	207.20	Terbium.....	Tb	159.2
Lithium.....	Li	6.94	Thallium.....	Tl	204.0
Lutecium.....	Lu	175.0	Thorium.....	Th	232.15
Magnesium.....	Mg	24.32	Thulium.....	Tm	168.5
Manganese.....	Mn	54.93	Tin.....	Sn	118.7
Mercury.....	Hg	200.6	Titanium.....	Ti	48.1
Molybdenum.....	Mo	96.0	Tungsten.....	W	184.0
Neodymium.....	Nd	144.3	Uranium.....	U	238.2
Neon.....	Ne	20.2	Vanadium.....	V	51.0
Nickel.....	Ni	58.68	Xenon.....	Xe	130.2
Niton (radium emanation) Nt		222.4	Ytterbium (Neoytterbium) Yb		173.5
Nitrogen.....	N	14.008	Yttrium.....	Yt	89.33
Osmium.....	Os	190.9	Zinc.....	Zn	65.37
Oxygen.....	O	16.00	Zirconium.....	Zr	90.6
Palladium.....	Pd	106.7			

## THE MEETING OF THE AMERICAN CHEMICAL SOCIETY.

The semi-annual meeting of the American Chemical Society, held at Chicago during the week of September 6th, was rich in achievement and splendidly attended. Over twelve hundred members representing every section of the country were in attendance.

As usual, all of the business of the Society was transacted by the Council, which met Monday afternoon and evening, September 6, at the University Club. The most important matters of business transacted were: Changing the name of the Division of Pharma-



ceutical Chemistry to Division of Chemistry of Medicinal Products; changing the name of the Carney's Point Section to South Jersey Section; going on record as favoring the purchase of Liberty Bonds for investment purposes; fixing the date of the spring meeting at Rochester, N. Y., for the week of April 25th; selecting Pittsburgh as the fall meeting city unless arrangements can be made for a joint meeting of the Canadian and British Societies of Chemical Industry with the American Chemical Society at New York either preceding or following the Chemical Exposition in New York next September; cautioning local sections of the Society against affiliations with local engineering organizations which may involve the parent body in matters of public policy favored by engineers but not of interest to chemists; re-election of the present editors of the three journals of the Society to serve for one year; authorizing the appointment of a committee of thirteen to coöperate with the Chemical Warfare Service along lines of research, development, production and physiological questions; re-endorsing the position taken at the last meeting in favor of the dyestuffs protection bill still before Congress; increasing the annual dues from \$10 to \$15 with the proviso that undergraduate and graduate students may secure such membership for \$10 per annum.

Meetings of the various divisions of the Society were held at the University of Chicago, Wednesday and Thursday, September 8 and 9.

The program of the Division of Chemistry of Medicinal Products included papers on the newer anti-spasmodics of the benzyl benzoate type. Reports were made by various investigators on benzyl succinate, benzyl esters of salicylic acid, and benzyl esters of the higher fatty acids. There seemed to be an undercurrent of opinion that benzyl benzoate could be improved upon and it is evident that many manufacturers are engaged in research work along this line.

An entire afternoon was devoted by this section to a discussion of methods of coöperation with the National Research Council. Dr. Wilder D. Bancroft, of the Council, advocated the framing of a complete program of research along medicinal chemical lines, after which the aid of the Council could be counted upon in carrying out the work outlined. Dr. C. H. Herty expressed the hope that an institute for research, along the lines of developing synthetic medicinal compounds, be organized in the near future and mentioned the possibility of securing financial aid for this purpose through the Chemical Foundation. After considerable discussion on this subject

it was decided to appoint a committee to digest the papers and view-points expressed at this meeting and formulate some definite plan of research. The following committee was appointed: J. M. Francis, chairman; F. R. Eldred, Edward Kremers, Mr. St. John and H. V. Army.

The question of controlling the entry of narcotic drugs through Pacific Coast ports was also discussed and the following committee appointed to consider the matter and report to the Board of Directors of the Society: Prof. W. F. Rudd, chairman; E. R. Carter and F. R. Eldred.

The division re-elected Dr. C. E. Caspari, of St. Louis, chairman, and Edgar R. Carter, of Indianapolis, secretary. Other officers elected were W. F. Rudd, vice-chairman; Messrs. Taylor and R. P. Fischelis, members of the executive committee.

The Society held several general sessions at which papers of popular as well as scientific interest were presented, the presidential address of Wm. A. Noyes on "Chemical Publications" being of particular interest.

The entertainment features were elaborately planned and well executed, a notable feature being the many visits to various industrial institutions in and near Chicago.

R. P. F.

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## THE PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE.

### ABSTRACTS FROM THE MINUTES OF THE SEMI-ANNUAL MEETING.

The semi-annual meeting of the Philadelphia College of Pharmacy and Science was held September 27, at 3 P.M. President Howard B. French presided and thirty members were present.

The amendments to Article I of the Constitution and Article XII of the By-Laws as presented at the June meeting, were read and adopted.

The report of the Committee on Nominations was presented.

Dr. Robinson for the "Medical Section of the Alumni," reported that a preliminary meeting had been held, views exchanged and various plans proposed—one most favorably received was to have a luncheon in the near future and then organize for effective work.

Joseph W. England reported for the Committee on Memorial Resolutions on the decease of Edwin M. Boring; reported they had

completed their work and the engrossed resolutions were on the table for the inspection of the members.

George M. Beringer reported that the family of Mr. Boring had donated to the College almost a complete set of the AMERICAN JOURNAL OF PHARMACY, and moved that the thanks of the College be tendered for this valuable donation. So ordered.

*Election of Trustees.*—Messrs. Stewart, Gano and Harrison were appointed tellers.

The Committee on Nominations in submitting a list of nominees made the following statement: "Owing to the Amended Charter taking effect at this election, your committee, acting under instructions from the solicitor of the College, Edgar S. McKaig, Esq., asked for and received resignations from nine members of the Board of Trustees to take effect September 27. This was done to conform to the decree of the court by making it possible to elect twelve members of the Board of Trustees at this election." (Twelve more are to be elected in March, 1921, when the resignations of the remaining six members of the old Board of Trustees will be asked for.)

These nine resignations and three whose terms had expired September 27 (together with an unexpired term caused by death) created thirteen vacancies, to be filled by electing five for one year, four for two years, and four for three years.

While the ballots were being counted, Prof. E. F. Cook, the Executive Secretary of the Centennial Committee submitted a lengthy report of the work that had been done, an abstract of this report is given.

The Executive Chairmen are:

On Site, President Howard B. French.

On Contributions, Dr. R. V. Mattison.

On Historical Data and Centennial Volume, George M. Beringer.

On College Membership, J. C. Peacock.

On Publicity, Robert P. Fischelis.

Each of these chairmen will be supported by a committee which is yet to be announced.

The General Committee on the Centennial, so far as arranged, is as follows:

All officers of the College.

All members of the Board of Trustees.

All members of the Faculty.

Pharmacists: Men, M. D. Allen.

Women, Mrs. W. E. Lee, Mrs. C. H. LaWall.

Army, To be selected.

Navy, Dr. W. T. Minnick.

Physicians, Dr. W. D. Robinson.

Wholesale Druggists, Walter V. Smith.

Chemical Manufacturers, Dr. George D. Rosengarten.

Pharmaceutical Manufacturers, Milton Campbell.

Editors and Journalists, E. G. Eberle.

Analytical Chemists, Charles E. Vanderkleed.

Members of the State Boards of Pharmacy, L. L. Walton.

Salesmen, To be selected.

Students, To be selected.

The president of the college is to be chairman of this General Committee.

The United States has been divided into districts. Some states will have one district, some two districts, some three districts. Pennsylvania will have many districts, as also Philadelphia.

As the campaign develops and sufficient publicity material has been issued from the central office, the district committees will be asked to do some local work, and in the final month will be expected to make personal visitations, as far as possible, in an effort to secure contributions. Posters, descriptive booklets, circulars or other booklets will be issued.

*Alumni Addresses.*—In January of last year a request was sent to all alumni asking for biographical sketches. About 1800 were returned; a second appeal brought about 800 more. There are about 500 sketches received about 10 years ago. Many of these are no longer living. The material, however, is most valuable for the Historical Volume. There is a total of about 5,000 graduates from whom addresses are available, but the biographical sketches received represent only about one-half of this number.

*Centennial Week.*—It is proposed that Commencement Week in 1921 will be utilized for the Centennial celebration. The Pennsylvania Pharmaceutical Association meets in Philadelphia during the same week. A dinner at which class organizations will be present in large numbers will probably be a leading feature of the week's celebration.

*Site.*—The Committee have had the question of site under careful consideration, and it is hoped will be ready to report specifically in a short time.

The report was ordered entered and filed.

The deaths of Richard W. Cuthbert, a member of the College since 1872, and of Miss Jamella Fox since 1918, were announced.

George M. Beringer offered the following as a minute expressing the position of the College on the subject of illicit sales of narcotic drugs and alcoholic beverages and moved that it be adopted, spread upon our minutes and copies sent to the Government officials charged with enforcing the laws and to the medical and pharmaceutical press and to the newspapers.

The correction of alleged abuses in the drug and apothecary business was the principal reason assigned for the meetings of Philadelphia apothecaries in historic Carpenters Hall in 1821, that resulted in the incorporation of the Philadelphia College of Pharmacy. Since its inception this institution has always maintained the highest ideals of the moral obligation and the professional responsibilities devolving upon pharmacists, in the discharge of their duties to society. It has aimed to inculcate in its students and members a code of ethics in keeping with these ideals.

The laws enacted by Congress and the various Legislatures for the purpose of limiting the sale and dispensing of narcotic drugs and alcoholic beverages to strictly medicinal uses, have placed additional and grave responsibilities upon the pharmaceutical profession and the drug trade. Alcohol is the most important raw material of the drug and chemical industries and of necessity, in one way or another, enters into practically every operation of the pharmacist. It is the opinion of this College that the dispensing of all potent drugs, including narcotics and alcoholics, should be restricted to bona fide medicines and that the distribution of these should be exclusively a part of the professional duty of registered pharmacists.

The Philadelphia College of Pharmacy and Science realizes that with its amended charter and wider educational scope it retains fully its position of responsibility as the oldest pharmaceutical society in America and as a leading exponent of professional pharmacy. *Be it Resolved*, by the members in meeting assembled that they call upon every pharmacist to maintain faith with the Government and to demonstrate by his strict observance of the narcotic

and prohibition laws that the confidence of Congress and of the Legislatures in the integrity and honor of the pharmaceutical profession has not been misplaced. We denounce infractions of these laws not only as a menace to public welfare but likewise as inimical to our entire profession and believe that the violators who thus debase their calling merit the extreme penalties of the law and elimination from pharmaceutical associations and practice.

Dr. P. S. Stout added that the physicians present endorse these resolutions and pledge hearty coöperation in carrying out the provision mentioned, and the resolutions were unanimously adopted and directed to be given the widest publicity.

Prof. C. B. Lowe for Mr. E. S. Gatchell presented a copy of the first edition of the United States Dispensatory. The thanks of the College were voted to the donor.

The tellers reported as the result of the election for trustees that W. Duffield Robinson, George M. Beringer, Jacob M. Baer, Richard M. Shoemaker and H. K. Mulford had been elected for one year, and Joseph W. England, Otto Kraus, O. W. Osterlund and Samuel P. Sadtler had been elected for two years, and Wm. L. Cliffe, Russell T. Blackwood, Benjamin T. Fairchild and Walter A. Rumsey had been elected for three years.

Prof. LaWall, for Mr. Norman Dean, presented several old articles of pharmaceutical apparatus to the College. A vote of thanks was tendered the donor.

C. A. WEIDEMANN, M.D.,

*Secretary.*

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## CURRENT LITERATURE.

### SCIENTIFIC AND TECHNICAL ABSTRACTS.

DISTRIBUTION AND MIGRATION OF COPPER IN PLANT TISSUES.—Copper is universally distributed in all plants. By means of the very delicate zinc-copper ferrocyanide reaction the authors have been enabled to follow its distribution in various organs of the same plant. As the result of a great number of determinations on nearly thirty different species, including common trees, shrubs, culinary vegetables, fruits, and herbs, it is found that copper occurs in all parts of the plant. At the same time, it is not evenly distributed, but is found on those parts which possess the highest vital activity. Speaking generally, apart from the process of ripening of the seed,

the organs which dry up in the process of aging part with a considerable portion of their copper, which is transferred to the actively growing tissues with the reverse material. Thus, in shrubs and trees the buds are richer in copper than the wood or the bark. In evergreens the fresh younger leaves contain more copper than the older leaves. It is, moreover, evident that this increase of copper is not due merely to concentration of the juices by evaporation. In this respect the accumulation of the metal in certain organs is of quite a different order from that of the increase of certain inorganic salts, such as silica and calcium compounds. In the case of the ripening of fruits there is an evident concentration of copper in the seeds. In leguminous plants the amount of copper present in the green immature seeds is notably greater than that in the pericarps. As ripening proceeds this increase becomes more and more evident in the former. This is directly opposite to what is observed in the case of calcium salts, which are found to accumulate in the pericarps and also in dead or mature leaves. Moreover, more copper is found in the albumen or the decorticated cotyledons than in their envelopes; in the kernel than in the shell of nuts; and in the seeds than in the pulp of fleshy fruits. All these facts are in agreement with what is observed during the period of growth, when copper is transferred to the most active tissues. It would appear, therefore, that copper is in some way intimately connected with the vital processes of the plant. At present it is not possible to state what part the metal may play; but the inference is permissible that it is not unimportant.

(L. Maquerme and E. Demoussy, *Comptes rend.*, 170:87, 1920; through *The Pharm. Jour. and Pharm.*, April 17, 1920.)

STAINING TECHNIC FOR MALARIA PLASMODIUM.—Gutiérrez describes experiences with the different staining methods in vogue to decide which method is the most practicable and reliable. His final conclusion is in favor of the Tiedmann technic, slightly modified. A 1 per cent. solution of methylene blue in methyl alcohol is made, and a similar solution of eosin, and these are kept in dark colored vials. When ready to use, 10 Gm. of each solution and 10 Gm. of methyl alcohol are mixed, and 10 or 15 drops of the reagent mixture are poured on the smear of blood dried in the air. Then 20 or 30 drops of neutral, filtered water are added immediately, and the slide is tilted to insure the complete blending of the stain and the water. In one and one-half minutes—counting from the moment

the stain had been dropped on the specimen—the preparation is rinsed rapidly with water and dried with blotting paper, when it is ready for examination under the microscope. The water used does not have to be distilled water but it must be neutral; he prefers rain water for the purpose. Filtered water from any source can be used, provided that it is neutral. He tests for this by adding a small amount of pulverized hematoxylin to a test-tube containing 100 Cc. of the water and agitating gently. If the water turns yellow, this shows acidity, while a deep violet tint indicates that it is alkaline. A light violet tint indicates that the water is neutral and suitable to use. By adding a few drops of a 1 per cent. solution of sodium bicarbonate to the water and then a little more hematoxylin, comparing the tint with a control tube, the neutral reaction can soon be realized. This staining technic shows up all the forms of the plasmodium of malaria and other parasites of the blood, and it is excellent also for the differential leukocyte count. In conclusion he emphasizes that with this simple and reliable technic any practitioner can examine blood specimens, himself, without expensive equipment or relying on a distant laboratory. (From *Porto Rico Medical Assoc. Bulletin*, San Juan, Mar. 1920, 14, No. 125; through *Jour. Amer. Med. Assoc.*, May 1, 1920.)

**STABLE VITAMIN PRODUCT.**—Dubin and Lewi prepared a stable vitamin product, designated, "V." An analysis shows the chief components to be calcium, expressed as calcium oxide, 10 per cent.; phosphorus, 15 per cent.; nitrogen, 3.5 per cent.; fat, 2.5 per cent.; iron, 0.3 per cent.; silicates 5.6 per cent.; moisture, 10 per cent. The remainder goes to make up the rest of the phytin molecule—the main constituent of the product—which is double calcium and magnesium compound of inosite phosphoric acid. Owing to the method of preparation and to the results of experiments with normal and polyneuritic pigeons, normal and scorbutic guinea-pigs and finally with children presenting evidence of malnutrition, marasmus and rickets—a marked acceleration in the rate of growth having been obtained, particularly in the children—it is established that the product contains antineuritic, antiscorbutic and antirachitic vitamins. It is felt by the authors that until such time as the vitamins shall have been isolated and their chemical composition determined, their vitamin preparation is an admirable substitute and may be used with confidence in such a manner as described by Voegtlin.



It is not intended as a substitute for any method of treatment nor is it meant to be used in infant feeding only. Rather it is intended to be a valuable aid whenever its use is indicated. At the same time, it should not be lost sight of that the diet must contain sufficient protein, fats, carbohydrates and mineral salts and that the caloric value must be adequate for the needs of the individual. (From *Amer. Jour. of Med. Sciences, Phila.*; through *Jour. Amer. Med. Assoc.*, May 29, 1920.)

CAUSES OF RANCIDITY OF COCONUT OIL.—Two-year storage tests were made by Perkins on thirty samples of edible coconut oil. The results were in general agreement with the accepted views of rancidity and its causes. The action of light was found to be a powerful, but not necessary, factor in the production of rancidity. Enzymes from the fresh coconut meat had some effect on the keeping qualities of the oil, but sterilization was of doubtful benefit. An oil of low initial acidity remained sweet during two years' exposure to air and light. The measurement of rancidity is discussed briefly. (From *Philippine Jour. of Science, Manila*; through *Jour. Amer. Med. Assoc.*, May 22, 1920.)

STERILIZATION OF DRINKING WATER.—Among the chemicals investigated by De Blasi he found silver fluoride most effectual, but it required a comparatively strong solution and contact of an hour to completely sterilize the water. The water is rendered limpid afterward by addition of sodium thiosulphate. Cattle and horses drink water containing up to 1 : 10,000 of the silver fluoride (*tachiolo*) without reluctance or apparent harm, he adds. His research with sodium hypochlorite and certain other chemicals merely confirms what others have published. (From *Annali d'Igiene, Rome*; through *Jour. Amer. Med. Assoc.*, May 22, 1920.)

RAPID METHOD FOR THE DETERMINATION OF SULPHUR IN PETROLEUM OILS.—A. W. Christie and C. S. Bisson (*J. Ind. and Eng. Chem.*, 12: 171-172, 1920).—After the combustion of 0.5 to 0.6 Gm. of the sample in a calorimetric bomb with oxygen under a pressure of 30 atmospheres for the determination of the calorific value, the whole of the sulphur present in the oil has been oxidized to sulphuric acid. The contents of the bomb are washed through filter-paper into a 250 Cc. beaker, and the total acidity of the liquid is determined by titration. The solution is then made up to a definite

volume such that an aliquot portion of 25 Cc. will contain between 0.2 and 1.5 Mgm. of sulphur. A portion of 25 Cc. is measured out into a 300 Cc. wide-mouthed conical flask and acidified with one drop of dilute hydrochloric acid; 10 Cc. of a solution of benzidine hydrochloride (8 Gm. per litre) are added, the solution is shaken several times and allowed to stand for fifteen minutes or longer. The benzidine sulphate is collected in a Gooch crucible on an asbestos pad which has previously been treated with permanganate. The flask is rinsed three times with 5 Cc. of cold water, each portion being drained through the filter before the next is poured on. The asbestos pad and precipitate are then washed back into the original flask. One Cc. of 10 per cent. sodium hydroxide is added and the flask is warmed on the steam bath to dissolve the benzidine sulphate. Water is then added to bring the volume up to about 100 Cc. and 5 Cc. of concentrated sulphuric acid are added. The flask is placed on the steam bath and the solution is titrated hot with  $N/20$  permanganate until the red color fades slowly. An excess of 10 Cc. of permanganate is added, and heating on the steam-bath continued for exactly ten minutes. Ten Cc. of  $N/20$  oxalic acid are added, and as soon as the solution clears the titration is finished off with permanganate. The net consumption of permanganate is multiplied by the factor 0.041 to obtain the number of Mgms. of sulphur in the portion of original solution taken, this factor having been ascertained by the analysis of known solutions of sulphates. The results are essentially the same as those obtained by the gravimetric barium sulphate method. By using the entire rinsings of the bomb and concentrating to 25 Cc., accurate results may be obtained for oils containing only 0.1 per cent. of sulphur.—J. F. B. (From *The Analyst*, May, 1920.)

DETERMINATION OF VITAMINE.—R. J. Williams (*J. Biol. Chem.*, 42: 259–265, 1920).—The author has previously shown that the anti-beri-beri vitamine is necessary for the nutrition of yeast (*J. Biol. Chem.*, 38: 456, 1919), and this fact has been adapted to the estimation of the amount of vitamine present in solution. The rate of growth of yeast and the number of cells produced from one cell under standard conditions in eighteen hours is directly proportional to the amount of vitamine present.

The microscopical method, although yielding good results, is troublesome, and the following gravimetric method, which yields

more accurate results, has been adopted: The culture solution is of the usual type, containing cane sugar, asparagine, and various salts in water; 100 Cc. of this solution are placed in a 500 Cc. flask, the solution to be tested added, and the whole diluted with water to 110 Cc. The flask is plugged with cotton-wool, sterilized, and cooled to 30° C.

A suspension of fresh pressed yeast is made containing 0.3 Gms. in 1 litre of sterile water, well shaken, and 1 Cc. is introduced into the culture medium with a sterile pipette. The flask is placed in an incubator at 30° C. for eighteen hours, and the growth is then stopped by the addition of a little formalin. The yeast is filtered off through a weighed Gooch crucible, washed with water and alcohol, dried at 103° C., and weighed. The increase in weight over that of a blank determination is directly proportional to the vitamine solution added. The "vitamine number" of a material is defined as the number of Mgms. of yeast produced by the addition of its extract computed to 1 Gm. of the original material tested.

A discussion of the method is given, in which it is shown that the vitamine to be tested must be in solution, that foreign organisms present in the yeast offer no serious handicap to the working of the method, and that the usual substances present in vitamine solutions do not accelerate the growth of the yeast. (From *The Analyst*, August, 1920.)

CRITICAL STUDY OF METHODS FOR THE DETECTION OF METHYL ALCOHOL.—A. O. Gettler (*J. Biol. Chem.*, 42: 311-328, 1920).—The author has examined fifty-eight tests described in the literature by employing them with the distillates from a number of liquors to which known amounts of methyl alcohol were added ranging from nil to 30 per cent., in addition to five typical confiscated methyl alcohol liquors—a total of eighteen. The various reactions are divided into two groups: (A) Those in which the methyl alcohol must be oxidized to formaldehyde before testing, and (B) those in which the methyl alcohol is tested for directly.

On the whole, the former class yields more reliable and sensitive reactions, and is subdivided according to the class of compound with which the formaldehyde reacts—*e. g.*, phenylhydrazines, phenols, alkaloids, proteins, amines and miscellaneous substances.

The most satisfactory and sensitive reactions are: (a) Phenylhydrazine-ferric chloride-hydrochloric acid. (b) phenylhydrazine-

sodium nitroprusside-sodium hydroxide, (c) apomorphine-sulphuric acid, (d) peptone-ferric chloride, (e) reduced fuchsine-sulphuric acid and two crystal-producing tests, (f) *B*-naphthol-hydrochloric acid and (g) hexamethylenetetramine-mercuric chloride.

The five color reactions are sensitive to 1 in 200,000 but the crystal-forming reactions are reliable down to 5 per cent. of methyl alcohol and in solutions containing less than this amount the alcohol must be concentrated by fractional distillation.

Of the reactions classed under the heading of Group (B) only two out of twelve appear to be reliable and easily performed. These are: (*h*) boiling for seven hours with hydroxylamine and potassium hydroxide under a reflux condenser when cyanide is produced and may be tested for in the usual way and (*i*) determination of the sp. gr. and refractive index of the solution. The former test is very sensitive while the latter is reliable for not less than 5 per cent. of methyl alcohol and is liable to interference by the presence of substances other than ethyl and methyl alcohols and water.

Detection of methyl alcohol in liquors: 100 Cc. of the liquor are neutralized with sodium carbonate to phenolphthalein and slowly distilled until 50 Cc. of distillate are collected. This is divided into two portions of 30 Cc. and 20 Cc. the latter being tested directly by the above reactions (*h*) and (*i*). To the 30 Cc. portion of distillate 100 Cc. of 10 per cent. sulphuric acid are added followed by 6 grams of potassium dichromate and the whole allowed to stand ten minutes. The flask is connected to a condenser and distilled so that about 30 Cc. of distillate are collected in one hour. This distillate contains most of the acetaldehyde and is rejected and distillation then continued somewhat more rapidly until about 60 Cc. are obtained. This fraction which contains nearly all the formaldehyde is then tested by the above reactions in the following sequence: (*b*), (*c*), (*d*), (*e*), (*g*), (*f*). A definite reaction with one or two of these tests only may be due to foreign substances, but if methyl alcohol was originally present, all the results obtained will be positive.

Detection of methyl alcohol in tissues: 500 Gms. of tissue are finely ground and placed in a large distillation flask with 500 Cc. of water. Sulphuric acid is added until a distinctly acid reaction is produced, and the mixture is then distilled in a current of steam. Three hundred Cc. are collected, neutralized, and again distilled slowly, this distillate being oxidized as above, when subsequent

distillation gives all the formaldehyde in the first 40 Cc. The final distillate is then tested by the same reagents as given above under examination of liquors, omitting the hexamethylenetetramine-mercuric chloride test.

Full details are given for the preparation and employment of the various reagents, which are classed according to their reliability, sensitiveness, and ease of application. (From *The Analyst*, August, 1920.)

A SOURCE OF ERROR IN THE SULPHOSALICYLIC ACID TEST FOR ALBUMIN IN URINE.—Schall reports that sulphosalicylic acid when combined with urine containing large amounts of calcium produces a precipitate which so closely resembles albumin as to cause confusion. The precipitate is, however, denser than any sediment or other clinical findings. Control tests with other albumin reactions, heating, or previous dilution of the urine, serve to avoid diagnostic errors. (From *Munchener medizinische Wochenschrift*, Munich, February 6, 1920, 67, No. 6; through *Jour. Amer. Med. Assoc.*, August 28, 1920.)

COMPARISON OF RECENT STAINING PROCEDURES FOR TUBERCLE BACILLI.—Jötten and Haarmann commend their modification of the Spengler method for the demonstration of tubercle bacilli. After the smear has been stained in the usual manner with carbolfuchsin solution it is decolorized (twenty seconds) with a 15 per cent. nitric acid solution. It is then briefly rinsed and again treated for ten seconds with nitric acid; rinsed again and afterward counterstained for about thirty seconds in Spengler's picric acid-alcohol mixture (saturated aqueous picric acid and absolute alcohol, equal parts). The smear is again rinsed and allowed to dry and is now ready for microscopic study. Out of 170 sputum specimens the Ziehl-Neelsen method yielded fifty-nine positives and the Spengler original method gave sixty-one, whereas the modification just described furnished sixty-two positives. Furthermore, the average number of bacilli visible in the field was thirty-one for the modification, twenty-six for the Spengler original method and only thirteen by the Ziehl-Neelsen method. (From *Munchener medizinische Wochenschrift*, Munich, June 11, 1920, 67, No. 24; through *Jour. Amer. Med. Assoc.*, August 28, 1920.)

PURIFICATION OF BENZOIC ACID BY FRACTIONAL CONDENSATION.—Benzoic acid, made by the chlorination of toluene, is con-

taminated with small amounts of compounds chlorinated in the ring, the presence of which is most objectionable from the physiological point of view when benzoic acid is used in food products. While it is very difficult to remove these compounds by the ordinary methods of purification, benzoic acid practically free from chloro-derivatives was obtained in the Bureau of Chemistry by the use of a special apparatus. This apparatus consisted of a vessel in which the crude benzoic acid was placed. The vessel was immersed in an oil bath kept at a definite temperature. A blast of hot air was passed into the crude benzoic acid and the vapors coming off were conducted through a series of chambers, maintained at different temperatures. The least volatile chloro-derivatives separated out in the hotter chambers, whereas the more volatile benzoic acid collected in the colder chambers. (Max Phillips and H. D. Gibbs, *J. Ind. Eng. Chem.*, 12: 277 (1910); through *Jour. Franklin Institute*, May, 1920.)

ORIGIN OF PEPSIN.—Pavlovsky reports research which has apparently demonstrated the important share of the spleen in the formation of the gastric ferments, and that injections of spleen extract increase the quantity and improve the quality of the secretion in the stomach. Injections of fresh leukocytes and red corpuscles from the horse acted in the same way. All confirm the rôle of the spleen in normal digestion as well as in blood production, and sustain the principle that the secretion of an organ is perhaps the best stimulant to promote its secretory function. He gives the details of series of tests on dogs with a Pawlow gastric pouch, given an intramuscular injection of 25 Cc. of a 25 per cent. decoction of spleen tissue, the blood count recorded over long periods, and the units of gastric digestion. (From *Semana Medica*, Buenos Aires, Mar. 18, 1920, No. 12; through *Jour. Amer. Med. Assoc.*, Aug. 21, 1920.)

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#### NEWS ITEMS AND PERSONAL NOTES.

A. D. M. A. RESOLUTIONS ON THE DECEASE OF RICHARD C. STOFER.—In testimony of the high regard it entertained for its late President, Mr. Richard C. Stofer, the American Drug Manufacturers' Association recently adopted the following resolution on his death:

"RESOLVED, That it is with profound sorrow that the American Drug Manufacturers' Association learns of the demise of its beloved

President, R. C. Stofer, and that, while it offers to the bereaved family a sympathy that an appreciation of his lovable qualities makes heartfelt, it likewise offers them the consolation that is to be found in the thought that their beloved husband and father still lives in the good works he has left behind him, and in the cherished memories that his sterling manhood has instilled in all who were fortunate enough to know him."

**CINCINNATI COLLEGES AMALGAMATED.**—The amalgamation of the Queen City and the Cincinnati Colleges of Pharmacy has been announced and the joint classes are being conducted in the building of the Cincinnati College of Pharmacy.

The Cincinnati College of Pharmacy was founded in 1895. The institution was conducted as a corporation for many years, but some years ago all the stock passed into the hands of Professor C. T. P. Fennel, son of Professor Adolph Fennel, one of the founders, who had been teaching in the institution for many years.

The Queen City College of Pharmacy was founded by Dr. Frank Cain in 1912 and became a part of Lebanon University two years later. When the charter of that institution was taken over by Wilmington College the control of the Queen City College was also taken over, and it has been conducted in Cincinnati as the school of Wilmington College since that time. Dr. Cain was succeeded as dean by Dr. Caswell A. Mayo, formerly of New York, and it was largely through his efforts that the amalgamation was effected.

With the coöperation of Professor Fennel, the Ohio Valley Druggists' Association has begun a campaign to raise sufficient funds to take over the College and to furnish a permanent endowment.

**WOMEN PHARMACISTS AS TEACHERS.**—Mrs. C. H. LaWall (Millicent S. Renshaw, P.D., P. C. P., 1904), is now Director of the Pharmacy Laboratory in the Women's Medical College of Philadelphia. Her assistant is Mrs. Mary Vogel, a recent graduate of the P. C. P. Formerly these positions were respectively held by Catherine G. Musson, P.D., P. C. P., 1901, who retired on account of ill health after 12 years of service in this position, and Bertha Whaland, P.D., 1906, M.D., 1911, who has opened a sanitarium at Bridgeton, New Jersey.

## OBITUARY.

## RICHARD C. STOFER.

In the decease of Mr. Richard C. Stofer, for fourteen years president of the Norwich Pharmacal Company, Norwich, N. Y., who died at the Norwich Memorial Hospital on September tenth after an illness of several months, another prominent figure among manufacturing pharmacists has passed away.

Mr Stofer was born September 11, 1862, in Wilmington, Delaware, and was educated in Philadelphia. In 1882 he entered the employ of Keasbey & Mattison Company, chemical manufacturers, of Ambler, Pennsylvania, leaving them in 1892 to become superintendent and chief chemist of the Norwich Pharmacal Company. Later on he was made Vice-President, and in 1906 President; a position he held with honor to his company, and credit to himself, until his death.

During his twenty-eight years on the Norwich staff, he, more than any other one man, was instrumental in the growth of the house from a tiny business occupying a part of an old wooden piano factory, into a group of modern brick and concrete structures, containing many acres of floor space; from a concern comparatively unknown to one enjoying an enviable position among the half-dozen largest of its kind in the United States.

In local civic and philanthropic movements, he occupied a prominent place, serving from time to time as president or director of many organizations. He was also active in church and Masonic circles, a member of the American Chemical Society and of the American Pharmaceutical Association.

In the broader walks of pharmaceutical and industrial life, he was a figure of national prominence, filling, among many other offices, the dual rôle of President, for two years, of the American Drug Manufacturers' Association—an office regarded by many as the highest pharmaceutical honor in the United States—and as President of Associated Industries of New York State, made up of two thousand or more Empire State Industries, representing a capitalization of one and one-half billion dollars and a pay roll of ninety thousand employees.

Among the lesser offices to which he gave much of his energy and wisdom during the past few trying years, have been Director and Vice-President of the American Association of Pharmaceutical



Chemists, of which he was one of the founders, member of the executive committee of the National Drug Trades Conference, Director of the State Industrial Safety Council, member of the Advisory Council of the State Industrial Commission through appointment by Governor Whitman, member of the Council of National Defense, national counsellor to the United States Chamber of Commerce, etc.

He was always prominent in advancing uniform and just national drug legislation, preventing fraudulent practices in the drug trade and in insuring just rewards of initiative, discovery and invention in the drug and chemical field. His natural qualifications fitted him to become a leader in the industrial world and his close study of conditions, his sympathetic comprehension of the other man's viewpoint, his unfailing geniality and his democratic, unassuming ways earned for him the respect and good will of leaders in industry everywhere.

By his own efforts he climbed to the pinnacle of his life's ambition, occupying not only a commanding position in the pharmaceutical world, but what was, to him, of far greater importance, *viz.*, enjoying the respect, confidence and esteem of a nation-wide circle of warm friends.

Mr. Stofer is survived by his wife and two children, a daughter, Helen, and a son, Dr. M. W. Stofer, who is Medical Director of the company to which his father gave the best years of his life.

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#### BOOK REVIEWS.

"HOW TO PASS THE BOARD." By D. CHAS. O'CONNOR. 435 pages.  
Published by the Spatula Publishing Co., Boston.

Any one, who has come in contact with numbers of applicants for registration by a State Board of Pharmacy, must realize the eagerness with which many of these applicants will hail the appearance of a book with such a title.

Approaching the work with the needs both of the examiner and of the applicant in mind, and finding that the author cautions the student against preparing only to pass the examinations and not for the future, the reviewer is inspired with the hope that here, at last, may be a book of this character more worthy than those heretofore available. But, alas, the hope is blasted by a more extended survey.

A book of this kind can hardly be expected to be an example of literary perfection. It should, however, conform to the common

rules of grammar and composition. It is difficult to conceive of a well educated author writing, "Do *not* study heavy subjects *neither* directly after a hearty meal. Several instances of this appear in the book. Also, contractions like couldn't, haven't aren't, etc., are scattered throughout the work. Misspelling is abundant. Much of it, no doubt, is due to faulty proof-reading, but, the fact that certain technical terms are repeatedly misspelled leads to the suspicion that it is a short-coming of the author, as well. Abbreviations are thickly sprinkled through the text. They are not always uniform. For instance, Potassium Iodide is abbreviated Pot. Iod. on one line and on the next Pt. Iod. Hydrochloric Acid is abbreviated by the use of the symbolic formula, H Cl, also given as H C L, and even H. C. L. The last is the same as the currently used abbreviation for a prevalent economic condition. Such phrases as, "Lassar's Paste is a great seller in the big chain drug stores," occur with great frequency, are of no instructional value, and might well have been omitted in order to save space and avoid abbreviation.

Definitions are, in many cases, faulty. They should be more comprehensive. Destructive Distillation is defined as "the process of driving off the volatile portions from dry organic matter." According to this the sublimation of Benzoic Acid from Benzoin would be a process of Destructive Distillation. A Taenicide is stated to be a "medicine which kills worms," not being differentiated from a Vermicide, which is defined in the same words. In this connection it might be observed that faulty examples of definitions are frequently given. Chloral Hydrate is given as an example of a deliquescent substance. This flatly contradicts the statement of the Pharmacopoeia. In mentioning gums, the statement is made that "there are two official gums, Gum Camphor and Gum Arabic," a very unscientific grouping, and, at the same time, no mention is made of Tragacanth, which might be properly classed with Gum Arabic.

Chemistry, of all subjects, requires systematic treatment. There is, however, no attempt at a scientifically correct system of handling that subject.

The following are a few of the examples of inaccurate and misleading information distributed throughout the book:

"Dialyzed Iron is made by mixing a *solution* of Ferric Hydroxide with Ammonia Water," etc.

Narcotine is mentioned as a "Narcotic Principle."

Potassium Iodide is used in "Tincture of Iodine" to help dissolve the Iodine and *keep it from precipitating.*"

*Boiling* water is stated to be used to extract the Glycyrrhiza in making the Fluidextract. The official formula directs water and Ammonia Water.

Spirit of Camphor and others of this class are mentioned individually as "spirits."

The reasons for certain changes in official formulas, particularly in the N. F., are mere guess work, the logical reason being entirely overlooked.

"Caraway plant is a grain like wheat and oats."

"Lard is the fat from the hog's stomach."

Fluidextract of Malt is said to be official in the N. F.

"Rennin is the milk-curdling ferment of pancreatin."

"Colchicum is a small herb."

Saw Palmetto is described as "a shrub."

"Pomegranate is the dried stem and root."

Staphisagria is given as from a "larkspur tree."

Corn Silk is stated to have no official preparations, overlooking the Fluidextract.

Mucilage of Sassafras Pith is said to be used for dysentery and inflamed conditions of the stomach. The more important use as a delicate mucilage suitable for treatment of inflamed conditions of the eyes is ignored.

In discussing the treatment of strychnine poisoning, the statement is made that an "*emetic* of flaxseed tea, slippery elm tea is given."

A careful perusal of the book gives, at first, the impression that the author is a fairly well informed and efficient prescriptionist. Later, the conviction is borne home that he is woefully deficient in the thorough knowledge necessary to enable him to instruct and guide the type of student who will be most likely to use his book.

G. M. B., Jr.

LEGAL CHEMISTRY AND SCIENTIFIC CRIMINAL INVESTIGATION. By A. Lucas, F.I.C., Director Government Analytical Laboratory and Assay Office, Cairo. London, Edwin Arnold, 1920, pp. 181. Price, \$3.40.

The author of this interesting book upon an important subject is apparently well qualified by experience and training to contribute authoritative data upon a number of phases of legal chemistry.

The collection of notes, for the author disclaims any pretensions to completeness as a treatise, covers an unusually wide and entertaining range of topics, as will be evidenced by the following list of chapter headings:

Alcoholic Liquors, Antiquities, Blood Stains, Building Materials, Bullets and Other Projectiles from Firearms, Clothing, Counterfeit Coins, Damage to Crops, Documents, Dust and Dirt, Explosives and Explosions, Fibres, Finger Prints, Fires, Firearms, Foods and Drugs, Gold and Silver Wares, Haschisch, Poisons, Pollution of Water by Sewage, Robbery from Letters and Parcels, Stains and Marks, Strong and Rope, Textile Fabrics, Tobacco, Traps for Criminals.

There is an introduction containing much valuable practical information and advice concerning the reception of the article, the records necessary to be made, the manner of reporting results and the facts bearing upon the subject in general.

Throughout the entire book the author has drawn upon the information available from his personal experience and quotes freely and interestingly from his case records. Some of the data and descriptions have a markedly oriental flavor as might be expected from an author whose experience has been largely gained in Egypt.

A valuable feature of the book is the bibliography to be found in connection with each monograph or chapter. While admittedly incomplete it nevertheless contains titles and references not often seen.

The author's style is facile and expressive. His material is entertaining, besides being valuable. Some of the monographs are as interesting as episodes in the career of the mythical Sherlock Holmes and the only fault one has to find with the book is that it is too brief.

It is a valuable contribution to forensic chemistry and will undoubtedly be consulted by many scientific experts for data not to be found elsewhere.

C. H. LAW.

ANNUAL REPORTS OF THE CHEMICAL LABORATORY OF THE AMERICAN MEDICAL ASSOCIATION, Volume 12.—This is another valuable report emanating from the Chemical Laboratory of the American Medical Association. It again emphasizes the important functions of this adjunct to the A. M. A. established in 1906 and the value of the service rendered thereby.

The contents of this brochure of 112 pages is arranged in three

parts. Part I consists of reprints of a number of contributions from the Laboratory. Among these we consider of especial value the examinations of American-made synthetic drugs, such as procaine, barbital, holocaine, and cinchophen. In many of these the methods employed had to be original in the absence of official standards. The conclusions arrived at, "that American chemists were producing synthetic drugs formerly controlled by Germany and have thus declared their independence of German chemicals and from the evidence at hand the quality of American synthetics will be second to none," is indeed welcome and satisfying.

Part II contains reports abstracted from the *Journal of the A. M. A.* and from the Annual Reports of the Council on Pharmacy and Chemistry and these, as well as some of the articles in Part I, deal with the unwarranted and at times fraudulent claims made for proprietaries. These exposures should have a very salutary effect upon the practice of medication especially that of self-medication.

Part III contains reports not previously published. Among these important contributions we mention "Note on Melting Point of Acetylsalicylic Acid," "The Examination of Acriflavine and Proflavine," "The Examination of Commercial Barbital-Sodium," "The Examination of Luminal and Luminal-Sodium." Here also are given some additional reports upon proprietaries.

In each examination reported upon, the methods employed are reported in sufficient detail for the information of the chemist reader and the conclusions and deductions are set forth clearly. The methods employed at times are original and oft times ingenious and will prove valuable as suggestive to other analysts who have similar problems to cope with.

G. M. B.

P-W-R MANUAL. Published by Powers-Weightman-Rosengarten Co., Manufacturing Chemists, Philadelphia, Pa.—This book of 471 pages, with its clear type, good paper and binding and with rounded corners to its pages is noteworthy and exhibits a practical application of the printers' art. The contents of this book evidence the highest ideals. It is a commendable effort on the part of a manufacturing corporation to impart accurate information concerning its products, standards of quality, and methods of testing. The clear, concise and scientific method of presentation of the subjects demonstrates the reliability of the work.

Above all the impartial manner of the statements appeals to us.

Despite the fact that it is a private publication covering commercial products of the publishers, there is a total absence of any attempt to advertise their business and contrary to the customary procedure in such "house publications" nowhere throughout the text occurs any reference to trade interests or even a suggestion that preference should be given to their products. We esteem it all the more highly because of this exceptional character and altruistic attitude.

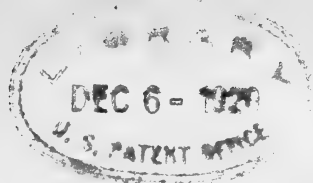
The major portion of the book is devoted to monographs in alphabetical sequence and in style copying somewhat that of the U. S. P. but more condensed and at times more directly to the point. The International Atomic Weights for 1920 are given in tabular form, although the atomic weights of 1915 had been used in the preparation of the book. For all practical purposes this is immaterial. We note that in this table sulphur is spelled "sulfur," but we are happy to note that elsewhere throughout the book the official spelling of the U. S. P. is closely followed even to the dropping of the final "e" from such words as dextrin and glycerin and the retention of the final "e" in words ending in "ine," "ide," etc. In these monographs the official chemicals and standards are designated as U. S. P. and the standards for technical grades are stated separately.

In the Appendix are given a number of important tables and data commonly needed by analysts in the examination of the chemical products treated of in the book and these handy references will add very materially to the usefulness of the work. The closing chapter on Poisons and Their Antidotes is a practical and terse presentation of another subject that may require the attention of the pharmacist or chemist at any moment and the advice of the first sentence, "*The first thing to do in case of poisoning is to call for a physician,*" should be heeded.

In this exemplary publication, this manufacturing chemical house has compiled much valuable information and despite their modesty and self-obliteration the service they have thus performed merits commendation and should bring to them evidence of approval as well as continued material support.

G. M. B.

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# THE AMERICAN JOURNAL OF PHARMACY

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NOVEMBER, 1920

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## EDITORIAL.

### TO WORK FOR ONE'S PROFESSION, A DUTY.

With the expulsion of our first parents from the Garden of Eden, came the command: "In the sweat of thy face shalt thou eat bread, till thou return unto the ground." So it was ordained as a perpetual law of the Omniscient that man, the highest of all created beings, must be sustained throughout his existence by his own labor. Despite the ages that have passed since the promulgation of this Divine edict, man, as yet, has formed but an imperfect conception of the creation known as *man* and of the perfection of this mechanism and the possibilities of the mental activity and physical energy stored within the human frame.

Labor applied in accordance with the Creator's injunction "to till," "to produce," and with the energy that will cause the worker to sweat, is the foundation of all achievement and the source of true happiness. He who fails in the application necessarily also fails to get out of his work any real satisfaction or enjoyment and will never know what true happiness is. Application of the God-given talents is "the thing that counts."

"Not what we have, but what we use;  
Not what we see, but what we choose—  
These are the things that mar or bless  
The sum of human happiness."

If one studies only the limited circle with which he is brought in contact in his daily routine, he will perceive a variety of characters and a diversity of actuating motives and, moreover, will obtain a new view of the proverbial perversity of the human nature. Doubtless, he will note the very large percentage of those that he meets who are engaged in the purely selfish chase after wealth. In this scramble after dollars, they appear indifferent to the higher ideals

of manhood and the obligations of true citizenship. A real estate dealer recently stated to the writer that his "aim was to get a big pile and to get it quick!" His sentiments and manner suggested that he might become a safe companion for a safe cracker. Then there is the type whose sole ambition is the seeking of notoriety and by one means or another these manage to keep continually in the lime light of public notice. Then there is that other large group composed of the shirkers and slackers who are forever playing the "let George do it" act. The world is to-day, possibly more than at any other period, cursed with these drones and buzzards whose failure to labor and produce constitutes a most serious world-wide problem. Less conversation and more perspiration is the lesson that is needed. Likewise, the misfits are in evidence; those who, after a fashion, are applying themselves to jobs unsuited to their mental or physical abilities and the enormous loss resulting thereby is another problem that society must sooner or later rectify. Our picture presents other heterogeneous types which we can leave to the imagination of the reader.

Nevertheless, despite this picture of the social condition, we are optimistic and believe that the world is slowly, yet surely, getting better and that fortunately there is an ever increasing proportion of its inhabitants who realize that within their respective spheres of labor they have a responsibility to society and are endeavoring to faithfully discharge same. The vocation is immaterial to this contention. Be it that of the professional man, banker, merchant, manufacturer, farmer, mechanic or day laborer, each has his share in the responsibility and his productive labor is but the service that he owes to society and is his expected contribution to the progress of the world. Work brings its own reward with advancement to the individual and enrichment of his country.

We would draw a sharp distinction between that service to society which is presumed to be rendered by every one and the duty which a member of a profession owes to that profession. The man or woman who enters upon a professional career should be imbued with the true professional spirit and, with a sense of the seriousness of the life's work, give thoughtful consideration to the obligations assumed in the practice selected. There is much more in a professional career than anticipated financial recompense and the pride of social position accorded thereto. Self gratification accomplishes nothing for the profession or of permanent benefit to the individual. The



ideals of the professions are upon a more ethical plane that does not contemplate such shallowness and selfishness. Unquestionably, there is need that these be maintained by a more exacting practice.

No person has rightfully a place in a profession that he does not love. The mere fact that he has succeeded in passing the required examinations for the diploma and the license to practice does not signify that he is enthused with the spirit and love of the profession and that its ideals can be safely entrusted to his care. It is far more essential that he possess that love for the sciences and associated labor of his profession that will impell him to assume his full duty as a faithful contributor toward scientific progress and the continued advancement of his profession. To Theodore Roosevelt is credited the pertinent statement that "every man owes some of his time to the upbuilding of the profession to which he belongs."

Altruism should be the guiding principle of the professions. We cannot selfishly live for self alone. We share in the enjoyments, pleasures and benefits resulting from others labors and so it becomes us likewise to contribute our full quota to the sum of human knowledge, public welfare and the world's progress. Especially is it incumbent upon the members of a profession that the duty to one's profession is discharged in accordance with opportunity and in the true ethical spirit. The following short poem beautifully presents the thought of the mutual enjoyment of the benefits of labor.

#### MY NEIGHBOR'S ROSE.

The roses red upon my neighbor's vine  
Are owned by him, but they are also mine,  
His was the cost, and his the labor, too,  
But mine as well as his the joy, their loveliness to view.

They bloom for me, and are for me as fair  
As for the man who gives them all his care.  
Thus I am rich, because a good man grew  
A rose-clad vine for all his neighbor's view.

I know from this that others plant for me,  
And what they own, my joy may also be,  
So why be selfish, when so much that's fine  
Is grown for you, upon your neighbor's vine?—*Gruber.*

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## THE THEORY OF PERCOLATION.

BY JAMES F. COUCH.

WASHINGTON, D. C.

The process of percolation stands at the very foundation of the art of Pharmacy for it represents the first operation in the preparation of a plant drug for medicinal use. The list of organic products is small whose manufacture does not involve percolation at some stage, usually the primary process, and so most of our drug compounds bear witness to the importance of this process. The percolator is a truer sign of pharmacy than the gilded mortar and pestle which so long directed the wayfarer to the apothecary shop, for the mortar suggests little more than the grinding together of the bitter ingredients of some heroic mixture or the powdering of some exotic and expensive root.

In the percolator, however, we can visualize the pharmacist's conquest of the crude *materia medica*; his ability to select and reject among the constituents of leaves and barks; the softening of the rigors of medication; development of certainty in dosage; and elimination of inert and deleterious matters from pharmaceuticals. Without percolation we should lose a valuable means toward the attainment of these ends.

From the very importance of the process we should expect that pharmacists should give it much attention and be fully informed on the various phases it presents; we find, however, a general neglect, particularly in recent years, of the whole subject. Indeed, it has too many times happened that pharmaceutical assemblies have been bored with discussions which attempted to penetrate farther into the mists which obscure our knowledge of the process. We find not only neglect, but in many cases, a lamentable ignorance of some of the first principles of percolation. We see gross lack of judgment in the choice of menstrua; carelessness in the details of packing the drug, of maceration, or of rate of percolation, and frequently no discrimination in the handling of drugs of widely different character. The work of extraction in pharmaceutical factories is too often left to men of small education who have but the slightest knowledge of the drugs they are extracting, whose ideas of the process are sometimes absurd, frequently extravagant, and generally erroneous, who do not appreciate the delicacy of the whole operation and are, therefore, crude

in manipulation and careless in detail. Nor is this lack of proper appreciation of the principles which underlie the process confined to such men; one questions the average pharmaceutical graduate in vain along lines which demand a broad, general survey of the subject.

The result of such conditions appears at once in the products. An examination of fluidextracts of different manufacture will reveal astonishing diversities in products made from the same drug and, presumably, by the same process.<sup>1</sup> Even in the case of the assayed preparations, the standard quantity of alkaloid or other active component is usually the only point of agreement.

It has, therefore, appeared desirable to survey our whole published knowledge of the process of percolation, widely scattered as it is throughout the literature and much of it inaccessible to the average worker; to examine it critically, state what facts appear definite, and particularly to direct attention to those questions which have not been investigated or which have been left in such an indefinite condition that further research is necessary to answer them.

#### HISTORICAL DATA.

The beginnings of percolation as a pharmaceutical process have been traced in an earlier memoir<sup>2</sup> and do not need extended description in this place. It is there shown that the credit for the establishment of the process of percolation in pharmacy is due to the Boullays of Paris, who, in 1833, published their work on the process of displacement,<sup>3</sup> and detailed discussion of the previous work of Real, Cadet, Robiquet and others is included. The earliest American notice of the process is the quotation of M. Soubeiran's memoir on "displacement" in this Journal.<sup>4</sup> Augustine Duhammel,<sup>5</sup> was the first American to publish any account of an original examination of the process. He states that the process had been in extensive use in Germany, "and elsewhere" for twenty years and that E. Durand was the first to use

<sup>1</sup> Haussmann, *Proc. A. Ph. A.* 1895, 564; Lloyd, *This Journal*, Vol. 80, p. 39; A. Conrath, *Proc. A. Ph. A.* 1882, 545; Spenzle, *Proc. A. Ph. A.* 1882, 547; Linde *Ph. Centr.* 1894, 39; *This Journal*, Vol. 66, p. 141; C. L. Diehl, *Proc. A. Ph. A.* 1878, 681.

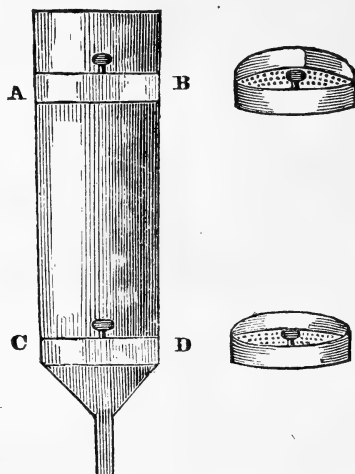
<sup>2</sup> *This Journal*, Vol. 91, 16, (1919).

<sup>3</sup> *Jour. de. Pharm.* 19, 2281, (1833); 19, 393, (1833).

<sup>4</sup> *This Journal*, Vol. 8, 221, (1836).

<sup>5</sup> "Boullay's Filter and System of Displacement with Observations Drawn from Experience." *This Journal*, Vol. 10, 1, (1838).

the process practically in this country. This memoir was followed a year later by "Observations on the Method of Displacement" by Augustine Duhammel and William Procter, Jr.<sup>1</sup> in which the advantages of the new process are clearly stated and its adoption is recommended.



Boullay's Original Displacement Apparatus

At C-D was placed a metallic diaphragm pierced with holes and provided with a handle and fitting accurately, designed to prevent the escape of the drug. At A-B a similar sieve was placed, intended to hold down the drug and scatter the liquid over the surface.

Percolation was then made official in two pharmacopoeias, the Edinboro pharmacopoeia of 1838 and the U. S. P. of 1840, published in 1842.<sup>2</sup>

Percolation quickly became a popular process in the United States; it does not appear to have attracted as much attention in any other country if we can be guided in judgment by the absence of more than scattering comments upon it in the foreign journals. American pharmacists, however, quickly perceived its advantages and began to study and apply the process. In 1847, E. T. Ellis<sup>3</sup> and Wm. Procter, Jr.<sup>4</sup> published formulas for the fluidextracts of Valerian, and Rhubarb and Valerian, respectively, and these papers were followed by published formulas for various other fluidextracts by Proc-

<sup>1</sup> This Journal, Vol. 11, 189, (1839).

<sup>2</sup> This Journal, Vol. 14, 125, (1842).

<sup>3</sup> This Journal, Vol. 19, 83, (1847).

<sup>4</sup> This Journal, Vol. 19, 182, (1847).

ter, Savary, Taylor, and others which gave evidence of intelligent comprehension of the principles involved in percolation and careful study of the drug and the menstrua suitable for its extraction.

The critical study of the process of percolation began in 1858 with Squibb's first paper,<sup>1</sup> although one critical commentary, that of Deane,<sup>2</sup> had already been published. For the next twenty-five years Squibb frequently contributed critical essays on percolation to the periodical literature. Procter, Maisch, Diehl,<sup>3</sup> Redwood,<sup>4</sup> Signoret,<sup>5</sup> Parrish,<sup>6</sup> Graham,<sup>7</sup> A. B. Taylor<sup>8</sup>, McIntyre,<sup>9</sup> Remington<sup>10</sup>, Moore,<sup>11</sup> Robbins,<sup>12</sup> and J. U. Lloyd supplemented and extended the work of Squibb. Lloyd appears first in 1877<sup>13</sup> and within a few years was easily the leader in this field of investigation. He has devoted much of his time during the past forty years to a study of percolation and the conditions affecting the process and its products. We owe by far the larger proportion of our knowledge of extraction to his patient industry and unselfishness.

Early in the Sixties, Squibb interested himself in the question of economy of alcohol in percolation<sup>14</sup> following the increased price of that solvent due to federal taxation. This study led to the development of his famous "repercolation" process<sup>15</sup> and led to a controversy that stimulated investigation and developed page after page of most valuable observations and deductions. The process of Squibb was not made official in the U. S. P. until the ninth revision (1916) although permission to use it was given in earlier revisions. It was considered that the complicated manipulations of Squibb's method were not suited for general pharmaceutical use<sup>16</sup> although it was admittedly an improvement.

<sup>1</sup> This Journal, Vol. 30, 97, (1858).

<sup>2</sup> *Pharm. Jour.* Vol. 1, 61, (1841).

<sup>3</sup> This Journal, Vol. 41, 337, (1869).

<sup>4</sup> *Pharm. Jour.* Vol. 23, 523, (1864).

<sup>5</sup> This Journal, Vol. 33, 319, (1861); from *Répertoire de Pharm.*

<sup>6</sup> This Journal, Vol. 31, 327, (1859).

<sup>7</sup> This Journal, Vol. 31, 354, (1859).

<sup>8</sup> This Journal, Vol. 42, 150, (1870).

<sup>9</sup> This Journal, Vol. 45, 210, (1873).

<sup>10</sup> This Journal, Vol. 46, 7, (1874).

<sup>11</sup> This Journal, Vol. 46, 497, 551, (1874).

<sup>12</sup> This Journal, Vol. 50, 329, (1878).

<sup>13</sup> *Proc. A. Ph. A.* 1877, 408.

<sup>14</sup> *Proc. A. Ph. A.* 1865, 201; This Journal, Vol. 38, 109, (1866).

<sup>15</sup> *Proc. A. Ph. A.* 1867, 391.

<sup>16</sup> This Journal, Vol. 41, 295, (1869).

Since the Seventies, a large number of memoirs bearing directly on the problems of percolation has been published and, of these, the larger proportion has resulted from the work of American pharmacists. The behaviors of different drugs in percolation have been compared, the effects of altered conditions studied, the factors which govern the permanence of the products investigated, new menstrua experimented with, much analytical data accumulated, and a host of new apparatus and methods developed and proposed. All of this work shall be considered in detail in the course of this survey and with this, we terminate the brief historical sketch, which to develop more fully would carry us into discussions which properly belong under other headings.

#### DEFINITIONS.

The term percolation, as generally used in this country, may be defined: a continuous process for the selective extraction, by a suitable solvent or mixture of solvents, of the soluble constituents of a mixture of substances part of which are insoluble in the solvent selected, conducted in such a way that the solvent travels through the mass to be extracted, from one surface of which the partially saturated solution is removed while fresh solvent is admitted at the opposite surface. The process is carried out in an apparatus called a percolator, of various designs and made of various materials for special purposes, usually of glass, shaped like a frustrated cone with the smaller end sharply constricted to a small tubular opening which may be fitted with a stopcock. In pharmaceutical practise the material percolated is usually called a drug and the solvent used is termed the menstruum. The solution as it runs from the percolator is known as the percolate, its dissolved matter is termed the extract, and the exhausted drug which remains in the percolator at the conclusion of the process is called the marc. The soluble constituents of the drug before their appearance in the percolate are included in the term extractive. It appears desirable, for theoretical reasons, to make a distinction between the undissolved soluble material and that actually in solution. Moreover, as there is frequently a chemical difference between the solution within the percolator and in contact with the drug, and the percolate, which is no longer in contact with the drug, it would seem advisable to distinguish between them by a specific name for the former. In this survey the term *percolate* will be used to specify the liquid found between the initial and terminal surfaces of the drug and in contact with it.

#### THE PERCOLATOR.

The design of the apparatus in which percolation is to be conducted has received a great deal of intelligent attention and in this narrow field, our knowledge may be regarded as very nearly complete. Nearly every thoughtful pharmacist has studied the subject and the result is that scores of new percolators have been suggested during the past eighty years. Many of these have involved innovations or radical changes in the process of extraction and are thus more related to some specific method than to general percolation. For this reason those percolators which substitute apparatus without affecting the process seriously will alone be considered in this section; the others will be analyzed when we discuss the unusual and special methods of percolation.

The early apparatus of the Boullays was essentially the cylindrical percolator sometimes seen to-day. Emil Mouchon of Lyons<sup>1</sup> substituted a funnel and the conical shape is first recorded in Gilbertson's apparatus.<sup>2</sup> The very tall, nearly cylindrical percolator was advocated by Oscar Oldberg in 1884.<sup>3</sup> The funnel shaped, the conical, and Oldberg's percolators are in common use to-day, the conical being the form most widely used. The essential difference between the three forms is, of course, the taper upon which depends the height of the column of drug and the number of contacts between each particle of drug and each aggregate of menstruum as well as the relative number of such contacts for the drug in the widest part and that in the narrowest part of the percolator.

Lloyd has shown<sup>4</sup> that the longer the column of drug is, the more concentrated the first portions of percolate are and he states two rules: first, that the height of both liquid and powder increase inversely as the square of the diameter of the percolator, and second, the contact between the liquid and powder increases inversely as the fourth power of the diameter of the percolator. The efficiency of the Oldberg design has also been confirmed by E. Moor, Jr.<sup>5</sup>

The importance of securing as much concentration in the early portions of the percolate as possible, other things being equal, is obvious. Nevertheless, for operations involving large amounts of

<sup>1</sup> Squibb, *Proc. A. Ph. A.* 1867, 391.

<sup>2</sup> *Pharm. Jour.* 1, 591, (1842).

<sup>3</sup> *Proc. A. Ph. A.* 1884, 388.

<sup>4</sup> *Proc. A. Ph. A.* 1879, 679.

<sup>5</sup> This Journal, Vol. 62, 333, (1890).

drug, as in the manufacture of several gallons of a fluidextract, the difficulty in unpacking a narrow, slightly tapering percolator is so great that the conical shape is used almost exclusively in such operations although its diameter is very much larger in proportion to its capacity. For such purposes a percolator as designed by A. B. Taylor<sup>1</sup> where the length is twice the largest and four times the smallest diameter will serve excellently.

The use of the funnel shaped percolator has provoked much discussion. The diameter of the percolator changes so greatly from the bottom upwards that the topmost layers of drug, which receive the fresh menstruum, are in contact with a much smaller amount per unit weight than the lower layers. The lower layers are acted upon by the most saturated menstruum the solvent powers of which are less than those of the fresh menstruum and, in the funnel percolator, the effect of the narrowing diameter is to force this partly saturated menstruum into longer contact with the drug than is the case higher up. The result is that, as the menstruum becomes laden with extractive and consequently weaker in solvent powers, it is forced to lie in contact with unit weight of drug for a longer time and this effect is distributed throughout the percolator in proportion to the diameter. The great advantage of the funnel percolator has been considered to be the fact that its taper will permit a drug which swells much during percolation to push its way upward instead of packing very firmly in the percolator as will happen in percolators of slight taper.

Campbell used the funnel percolator in his method for the preparation of fluidextracts without heat<sup>2</sup> which was approved by A. B. Taylor<sup>3</sup> and Kennedy,<sup>4</sup> although Reynolds,<sup>5</sup> King,<sup>6</sup> and Archibald<sup>7</sup> were unable to exhaust the drug thoroughly with the small quantity of menstruum permitted by Campbell's process. Taylor's experiments showed, however, that a very concentrated first percolate could be obtained with a funnel percolator if four days were allowed for the preliminary maceration. The use of this type of apparatus

<sup>1</sup> *Proc. A. Ph. A.* 1869, 390.

<sup>2</sup> *This Journal*, Vol. 41, 384, (1869); Vol. 42, 17, (1870).

<sup>3</sup> *Proc. A. Ph. A.* 1869, 390. *This Journal*, Vol. 42, 150, (1870).

<sup>4</sup> *This Journal*, Vol. 42, 62, (1870).

<sup>5</sup> *This Journal*, Vol. 41, 525, (1869).

<sup>6</sup> *This Journal*, Vol. 42, 29, (1870).

<sup>7</sup> *This Journal*, Vol. 42, 117, (1870).



was also advocated by Graham<sup>1</sup> and Cohen.<sup>2</sup> Squibb,<sup>3</sup> Parrish,<sup>4</sup> Lloyd,<sup>5</sup> and Remington,<sup>6</sup> have considered the more cylindrical shapes superior to the funnel and have discountenanced the use of the latter except for dilute preparations such as tinctures and wines.

There is one factor in this connection which has not been investigated and, indeed, which has too often been neglected in studies on extraction. That is the time factor. It is obvious that a given volume of menstruum will pass through a drug packed in a funnel much more rapidly than it will pass through the same amount of drug packed in a long, narrow percolator. Under such conditions we cannot expect the percolate from the funnel to contain as large a proportion of dissolved matter as that from the less tapered vessel, but we do not know what the relation between equal quantities of percolate from the two or three forms would be if the flow from the funnel were retarded to the same rate as that from the other apparatus, both delivering the same volume of percolate in the same time. Inasmuch as, within certain limits, the concentration of the first portions of percolate depend upon the length of time the menstruum has been in contact with the drug, the time factor is of great importance in comparing such percolators as these and, on account of the neglect of it, the whole subject demands further investigation.

In the hands of the inexpert or the careless operator the Oldberg or nearly cylindrical percolator will doubtless give more uniform results and a more concentrated first percolate such as is used for the reserved portion in the manufacture of fluidextracts. The conical form will prove nearly as efficient and has the advantage of being more easily unpacked.

Modifications of these three shapes have been introduced from time to time to adapt them to special purposes. Many forms of closed percolators have been described for use with volatile solvents such as ether, chloroform, benzine, or acetone, designed especially to minimize loss of the solvent through evaporation. Gilbertson's apparatus<sup>7</sup> was one of the first of these and it is very compact and

<sup>1</sup> This Journal, Vol. 31, 354, (1859).

<sup>2</sup> This Journal, Vol. 44, 8, (1872).

<sup>3</sup> This Journal, Vol. 38, 109, (1866).

<sup>4</sup> This Journal, Vol. 31, 327, (1859).

<sup>5</sup> *Proc. A. Ph. A.* 1877, 405.

<sup>6</sup> *Drug. Circ.* 1884, 148.

<sup>7</sup> *Pharm. Jour.* 1, 591, (1842).

ingenious. Army has also devoted his attention to this subject and has proposed several practical and serviceable forms,<sup>1</sup> in which the menstruum is kept out of contact with the air. That it is not necessary to have a tubular percolator in which menstruum enters at one end and percolate issues at the opposite end was shown by Squibb<sup>2</sup> with his tub percolator. Several other ideas<sup>3</sup> in percolator design were worked out by this indefatigable pharmacist and are worthy of the attention of every worker in the field of extraction.

Finally, a word may be said about the materials of which a percolator is constructed. Glass is the best material at hand and practically all small percolators are made of it. It possesses many advantages; transparency, so that the process may be closely watched and inequalities of flow, due to improper packing or accident detected, cleanliness; and minimum solubility, so that foreign matter is kept out of the product and undesirable reactions with the drug avoided. Its fragility, however, makes it impractical for apparatus larger than three or four gallon capacity unless it is reinforced as in the glass lined percolators of wood or metal. Lloyd's experience with glass percolators of ten gallon capacity confirms this statement.<sup>4</sup>

Large size percolators are commonly made of galvanized iron, some are made of tinned copper or iron, and some of stoneware. The galvanized iron percolator is strong, substantial, and inexpensive. It resists the corroding action of acid plant solutions very well but contaminates the percolate with small, nearly negligible amounts of zinc and iron. It is somewhat difficult to clean thoroughly and sooner or later rusts through and becomes unserviceable. Tinned iron percolators offer no advantage and rust through more quickly than the galvanized iron percolators. Iron percolators with enamelled inside surface are extensively used and are serviceable for most drugs. Tinned copper percolators are expensive and cumbrous and contaminate the percolate with small quantities of tin. Percolators of stone or earthen ware are frequently used for large batches of drugs which are to be extracted by strongly acid menstrua which would rapidly destroy metallic apparatus. A five or ten gallon stoneware jug from which the bottom has been removed makes a very useful percolator of this type. Plain wooden percolators are seldom used. They are

<sup>1</sup> *Proc. A. Ph. A.* 1892, 169.

<sup>2</sup> *Proc. A. Ph. A.* 1872, 182.

<sup>3</sup> *Proc. A. Ph. A.* 1878, 708.

<sup>4</sup> *West. Drugg.* 11, 159, (1888).

uncleanly, heavy, and not strong enough to withstand the great pressure developed by a swelling drug unless reinforced by many iron hoops.

#### THE DRUG AND ITS PREPARATION FOR PERCOLATION.

Plant drugs may be classified in a variety of ways but, for our purposes, their behavior toward solvents is the criterion of their relationships. From this point of view we may propose the following classification. I. Resinous drugs, *cimicifuga*, *cannabis*, balm of gilead, whose active principles are usually extracted only by strong alcohol. II. Terpene drugs, peppermint, *buchu*, thyme, whose active principle is a terpene or a terpene derivative demanding a menstruum rich in alcohol. III. Alkaloidal drugs, *gelsemium*, *nuxvomica*, *belladonna*; the menstruum depends upon the individual solubility of the alkaloid and the condition in which it exists in the plant. In general strong alcohol is needed for those plants which contain free alkaloids; dilute alcohol is employed where the alkaloid exists as a salt. Acid menstrua are often employed in the extraction of this class of drugs, *e.g.*, *ergot*, *lobelia*, *sanguinaria*. IV. Glucosidal drugs. The solubilities of the glucosides vary widely from insolubility to free solubility in water and dilute alcohol. Menstrua employed for this class vary from water in the case of *cascara* to alcohol for *strophanthus*. The majority of them may, however, be extracted with dilute alcohol. V. Oleoresinous drugs. *Pepper*, *parsley*, *aspidium*. These drugs are extracted with ether or the less expensive acetone, for the loss of solvent through evaporation may be quite large in spite of precautions. VI. Tannin-containing drugs. *Kino*, *rubus*, *krameria*. These drugs are extractible with water. However, aqueous solutions of their extracts are apt to gelatinize so the drugs are extracted with menstrua containing alcohol and glycerin is added to the first portions of percolate. Sometimes glycerin is used in the menstruum. VII. Saponin drugs, *quillaja*, *sarsaparilla*, *squills*, *senega*. The saponins are soluble in water and insoluble in cold alcohol. The menstruum usually used is diluted alcohol, the alcohol being employed as a preservative. Diluted acetic acid is of course, a favorite menstruum for *squills*. VIII. Mucilaginous drugs. A. *Elm*, *chondrus*; B. *senna*, *uva ursi*. These drugs are extracted in two ways according whether the mucilage is desired or not. A. Where the mucilaginous substance is to be extracted the drug is treated with hot water but is not usually percolated. B. If the mucilage is undesirable in the

product the drug is extracted with an alcoholic menstruum in which the mucilage is insoluble. In such cases the drug may be placed in another classification, senna in class IV and uva ursi in class II. IX. Acid drugs. Licorice, triticum, zea mays, mostly extractible with water, more easily with alkaline menstrua. Licorice is extracted with dilute ammonia. Rhubarb may be extracted with water but its content of mucilage presents practical difficulties so that dilute alcohol is usually employed. X. Miscellaneous drugs, requiring special treatment on account of individual peculiarities, prunus virginiana, gentian, quassia.

The class to which a drug is to be referred, then, will depend upon the nature and solubility of its active principle modified by the solubilities of undesirable ingredients which the plant may contain or by the exigencies of preserving the product. This classification is thus strictly pharmaceutical and very different from botanical or therapeutical systems. Drugs exhibit, however, such individualities that it is difficult to draw many generalizations about them.

This point is particularly true in the preparation of drugs for percolation. Squibb remarked<sup>1</sup> that the process of percolation differs materially with every drug and every menstruum used. The master of percolation varies the details of his process from beginning to end to suit the characteristics of the drug.

The extraction of a drug properly begins with the grinding of the crude material, proceeds through its moistening, maceration, packing and the actual percolation to the emptying of the exhausted marc into the dreg still. As all these steps are of considerable importance the following pages will bear a detailed discussion of each in order.

The fineness of the drug, that is the degree of comminution or the size of its particles, is a factor upon which depends, in no small measure, the success of percolation. Little has been published on this subject and that has been largely opinion based on practical experience and not upon critical experiment. The general agreement is that the finer the drug powder, the more efficient the extraction and the pharmacopoeia revels in number sixty powders. Squibb<sup>2</sup> thought a number 24 powder fine enough and Procter<sup>3</sup> allowed as coarse powder as Nos. 25 to 30 for mucilaginous drugs but preferred a fine

<sup>1</sup> *Proc. A. Ph. A.* 1869, 305.

<sup>2</sup> This Journal, Vol. 30, 97, (1858).

<sup>3</sup> This Journal, Vol. 31, 317, (1859).

powder.<sup>1</sup> Campbell<sup>2</sup> recommends a No. 40 powder. Lloyd<sup>3</sup> showed mathematically the probability of greater efficiency in extraction the finer the drug powder and Rosenwasser<sup>4</sup> developed the same conclusion. The following figures<sup>5</sup> for the yield of extract by

Menstruum.	Coarse Powder.	Fine Powder.
Cold water	32.94-39.82 per cent.	35.25-35.42 per cent.
Boiling water	40.19-41.22 "	38.68-38.91 "
Dilute alcohol	38.57-41.3 "	40.3 "
68 per cent. al.	36.32-39.31 "	39.1 "

maceration of gentian of different fineness and with various menstrua show a difference: Feil<sup>6</sup> reported 31.5 per cent. extract from gentian by percolation. The figures in the above table show more uniform results in extract yield from the finely powdered drug yet with every menstruum the coarse drug yielded more extract than the fine which is quite contrary to expectation.

In considering the differences in different degrees of fineness the time factor has again always been neglected. Any menstruum will pass more quickly through a coarse drug than through one that is finely powdered and is, therefore, in contact with the drug and able to exert its solvent action for a much shorter period of time. In my own experience I have known two weeks to elapse after flooding a percolator which contained 83 pounds of gentian in No. 60 powder before the percolate appeared. There is need of some careful investigation to furnish data in which all the factors are included. The results quoted above were obtained by maceration so that the time-contact factor is eliminated from the figures and they show a slight favor towards the coarse drug. If this time-contact factor were eliminated in percolating powders of the same drug of different degrees of fineness, by commencing the percolations after the same elapse of time after packing and adjusting the rate of flow of percolate to the same volume per hour for all cases the results furnished would contain no interfering factor and such data would serve as a basis for really valuable conclusions upon the relative merits of different degrees of fineness.

<sup>1</sup> This Journal, Vol. 36, 1, (1864).

<sup>2</sup> This Journal, Vol. 41, 384, (1869).

<sup>3</sup> *Proc. A. Ph. A.* 1879, 682.

<sup>4</sup> *Proc. A. Ph. A.* 1882, 519.

<sup>5</sup> *Proc. A. Ph. A.* 1906, 746.

<sup>6</sup> *Proc. A. Ph. A.* 1906, 433.

The general manufacturing practise at present is to use drugs ground to about a No. 12 powder. This is much coarser than the pharmacopoeia recognizes but is justified by the magnitude of the operations. There is present in such a drug powders of all degrees of fineness up to impalpability and this lack of uniformity is undesirable but unavoidable.

There is, too, a practical limit to the fineness of a powder which can be extracted with diluted alcohol. Consider a mucilaginous drug such as senna, gentian, uva ursi, or buchu, and in No. 60 powder. As the precolate descends through the drug it dissolves the extractive and also the drug moisture, an important constituent for practical reasons. This means that the alcoholic strength of the precolate is constantly diminishing and, if the column of drug be long enough, a point will be reached where its alcoholic strength is so low that the mucilage will begin to swell, preparing to dissolve, and, covering every particle of drug with a continuous slimy film, will clog the percolator, oppose the passage of the precolate, and probably terminate the process. In such a case one of two expedients must be resorted to in avoiding such an exigency; either the drug must be coarse enough to permit the passage of the precolate before it has become so dilute in alcoholic strength, or these large lots of very fine drugs must be extracted with menstrua of high alcoholic content. The variation of the menstruum is, in most cases, permissible only within very narrow limits and so the operator is forced to use coarser drugs for large batches. With pharmacopoeial quantities of 1,000 grams such factors do not enter into consideration, and it is possible that there exists a rational relationship between the quantity of drug to be extracted and the fineness required. Perhaps a No. 20 powder is to a No. 60 as a five litre product is to a one litre.

Another factor which must be considered is adsorption. How important this phenomenon is will be discussed later but in this connection it should be noted that adsorption resists extraction. It is an opposing force, and, being a surface phenomenon, increases with the enlargement of the drug surface, that is with increasing fineness of drug. It is known that in many cases the amount of substance adsorbed is less in alcoholic liquids than in aqueous solutions and the factor may disappear in strongly alcoholic percolates. Lloyd has established the fact of adsorption in pharmaceutical processes<sup>1</sup> and the literature on the physicochemical aspects of the phenomenon is

<sup>1</sup> *Proc. A. Ph. A.* 1885, 411.

voluminous, but much remains to be done before its rôle in percolation is made clear.

We cannot, therefore, conclude in favor of any one general optimum fineness for a drug. We may say that, the stronger the menstruum to be used is in alcohol the finer the drug may be powdered and as strongly alcoholic menstrea tend to shrink, instead of swelling, vegetable fibres and cells, the finer the drug the better in such cases. In general, the drug should be ground to as fine a powder as will be permitted by its character, the menstruum, the quantity being extracted, and the time available.



PROF. WILLIAM PROCTER, JR.

A pioneer advocate of the pharmaceutical application of percolation.

When the drug has been ground to the desirable fineness the next step in the process is the moistening of it and this brings up the selection of the menstruum. Here we find that a multitude of pharmacists have done very good and careful work for it was early recognized that not only the proper extraction but the permanence of the product depends upon the suitability of the menstruum. In choosing a menstruum the principles enunciated in the discussion of the classification of drugs must be borne in mind as well as the idea of the ideal menstruum which is such a one that will perfectly dissolve the active constituents and exclude undesirable ingredients furnishing a product that may be readily preserved.

The situation in respect to menstruum is excellent mainly because they have been chosen as a result of many experiments the conditions of which point definitely and unmistakably to the correct choice. Menstrua are usually chosen much in advance of any very detailed analysis of the drug plant and knowledge of the chemical and physical nature of the active constituents. Indeed, our lack of knowledge in this respect has been responsible for much empiricism in the application of menstrua. We have, however, succeeded in establishing a proper solvent for every important drug, though in most cases our products are not free from precipitation.

We are indebted to Procter<sup>1</sup> for initiating and prosecuting much of the work which has been done. Lloyd,<sup>2</sup> Savery,<sup>3</sup> Remington,<sup>4</sup> and a host of others have supplemented this work. Remington<sup>5</sup> and Squibb<sup>6</sup> have advocated the use of acetic acid menstrua, proposing to eliminate alcohol altogether in extracting certain drugs. Wulling<sup>7</sup> and Feil<sup>12</sup> supported the idea but Thompson<sup>9</sup> and Dohme<sup>14</sup> opposed it. As a result of this work acetic acid menstrua were directed by the 1900 pharmacopoeia. The preparations, however, failed to meet with the approval of physicians and were dropped in the last revision (1910).

The use of glycerin in menstrua as a preservative agent was early suggested by Taylor<sup>8</sup> and proved a distinct advance in fluidextract technique. Lloyd<sup>9</sup> recommends it for drugs which contain tannins and Lehman<sup>10</sup> regarded it valuable for drugs whose active principles are soluble in both alcohol and water but discards it for mucilaginous and resinous drugs. Moore<sup>11</sup> opposed the use of glycerin in menstrua

<sup>1</sup> This Journal, Vol. 19, 182, (1847); 23, 218, (1851); 24, 207, (1852); 26, 28, (1854); 25, 410, (1853); 28, 22, (1856); 31, 530, (1859).

<sup>2</sup> *Pharm. Rund.* 1889, 165.

<sup>3</sup> This Journal, Vol. 23, 119, (1851).

<sup>4</sup> This Journal, Vol. 46, 7, (1874). Cf. Squibb, This Journal, Vol. 39, 289; 398; 513, (1867).

<sup>5</sup> This Journal, Vol. 69, 121, (1897); 70, 543, (1898).

<sup>6</sup> This Journal, Vol. 71, 1, (1899); 72, 1, (1900).

<sup>7</sup> *Pharm. Era*, 1898, 796.

<sup>8</sup> *Proc. A. Ph. A.* 1908, 883.

<sup>9</sup> This Journal, Vol. 71, 67, (1899).

<sup>10</sup> *Proc. A. Ph. A.* 1904, 337.

<sup>11</sup> This Journal, Vol. 37, 50, (1865).

<sup>12</sup> *Proc. A. Ph. A.* 1877, 408.

<sup>13</sup> This Journal, Vol. 49, 346, (1877).

<sup>14</sup> This Journal, Vol. 46, 551, (1874).



unless it is a better solvent than either alcohol or water as it "interferes with percolation."

Beringer<sup>1</sup> has devoted much attention to the use of glycerin as a solvent and preservative. As a result of his work a new class of official preparations, the fluidglycerates, has been introduced. Ripp-toe<sup>2</sup> has shown that the fluidglycerates of digitalis and ergot are very much less active physiologically than the corresponding fluid extracts.

When the menstruum has been decided upon the drug is moistened with a portion of it and allowed to stand several hours to swell. This is done for practical reasons, *viz.*, to assist in packing, to allow a modification of the conditions of the drug constituents, and to insure the saturation of every particle of drug with menstruum so that the actual percolation may affect all the drug evenly. Some drugs need not be moistened,<sup>3</sup> as cisticifuga, cubebs and resinous or oleoresinous drugs which are extracted with alcohol, ether, chloroform, or petroleum ether and similar solvents and consequently do not swell in the percolator nor yield a viscous percolate. I believe, however, that it is better to moisten a drug before packing in all cases where it is practically and economically convenient.

A dry drug cannot be packed as evenly nor as firmly as one that has been moistened and, with uneven packing, the operator is doomed to get irregular extraction with probable incomplete exhaustion.

With certain drugs it is often desirable to modify the nature of the conditions in which the constituents exist. Alkaloidal drugs are often extracted with acid menstrua to increase the solubility of the bases and their rates of extraction. At other times it is desired to carry out the percolation in an alkaline medium, or perhaps, an alkaloid which exists as a salt in the plant is to be extracted with a menstruum, like benzol, in which the free alkaloid, but not its salt, is soluble. Or some treatment is required to render insoluble or to destroy an undesirable constituent as in the case of cascara sagrada.

In such cases it is usually best to make the modification at the time the drug is being moistened. Thus the quantity of acid, diluted with a portion of menstruum, is added all at once to the drug and evenly distributed through it. With ergot, lobelia, ipecac, etc., this is a stock method. In making alkaline a drug which is to be

<sup>1</sup> This Journal, Vol. 79, 410, (1907); Vol. 80, 525, (1908); Vol. 81, 475, (1909).

<sup>2</sup> This Journal, Vol. 81, 84, (1909).

<sup>3</sup> This Journal, Vol. 31, 317, (1859).

extracted with a solvent immiscible with water the common practice is to mix thoroughly with a solution of sodium or potassium carbonate, bicarbonate, or hydroxide, or ammonia and dry the mixture. Calcium hydrate, barium hydrate, magnesia or zinc oxide may be similarly handled.

Lloyd<sup>1</sup> has suggested bringing drugs to their natural moisture content by adding water to them and allowing them to swell before treating them with the menstruum designed to extract them. This has not been adopted. Indeed it would necessitate a thorough revision of all our menstrua except those which are strictly aqueous and would give us different products in many cases than those produced by the processes in present use. The resinous and terpene drugs would, of course, be most affected and while it is possible to extract many if not all of these drugs when they are fresh with dilute alcohols, it is doubtful whether the addition of water to the dried specimen, where the plant fluids have lost their solvent, would effect a re-solution of the resinous or terpene derivatives originally held in solution in the plant fluids. Probably the alcoholic menstrua used on such drugs would not dissolve the active principles until the added water had been nearly completely washed out.

An ingenious method of moistening small amounts of drug has been brought forward by Eberle,<sup>2</sup> who places the drug in a covered can, adds the menstruum and stirs. A few glass stoppers are then mixed with the drug and the whole is shaken. The stoppers prevent lumping of the powder and the drug is thoroughly moistened without evaporation of the solvent.

When the drug has been moistened it is customary to allow the mass to remain in a covered container until it has finished swelling. The extent to which drugs will swell as well as the time consumed in the process varies considerably and the variation is due somewhat to the menstrua employed in moistening them. In general drugs will swell more according to the density of their fibre, that is the more compact their cellulose structure is, the presence of mucilaginous or carbohydrate constituents, and the more aqueous the menstruum. The swelling is due to an imbibition of one or more of the constituents of the menstruum and drug particles appear to show much discrimination between the various solvents in use. Water is most readily and most largely absorbed by them, glycerin, acetone, dilute acetic

<sup>1</sup> *Pharm. Rund.* 1889, 165. *Proc. A. Ph. A.* 1890.

<sup>2</sup> *Drug. Circ.* 1900, 11. *Proc. A. Ph. A.* 1900, 398.

acid less, and benzol, alcohol, ether, chloroform, and petroleum ether are still less absorbed. When an hydro-alcoholic menstruum is used it is not uncommon for the drug to absorb more water than alcohol from the menstruum so that the composition of the liquid portion of the drug mass will be different from that of the unabsorbed menstruum, a phenomenon which may have an important effect upon percolation and which, like many others, needs investigation.

When the moistened drug has swollen sufficiently it may be passed through a coarse sieve to break up lumps, though this process is usually omitted, and then packed in the percolator.

The outlet of the percolator is plugged with something to prevent drug from being washed out with the percolate; cotton is used in small operations, excelsior for larger batches. The amount used is so small that the effect on the process due to it, while definite, is negligible. Covering the diaphragm with muslin, cheese cloth, or filter paper is a method quite commonly employed.

The packing of the drug in the percolator demands a certain amount of skill and the personal equation enters largely into it. Individual operators differ widely in the manner in which they pack the drug and it is difficult to devise directions which will lead to the same result in the hands of different men. It is usually stated that the drug should be packed evenly and firmly so as to lead to an even and not too rapid descent of menstruum through it without the formation of channels or regions of varying density in the same horizontal plane. The degree of firmness to be attained depends upon the character of the drug and the menstruum. In general, the looser the drug fibre and the richer the menstruum is in alcohol, the firmer the packing should be. All drugs, however, should be packed very tightly particularly if they have been allowed to swell.

Rosenwasser<sup>1</sup> suggested that greater force should be used in packing the upper layers of drug than was used on the lower layers since the force employed on the upper served also to compress the lower portions and, therefore, if a uniform force were to be used throughout the packing, the lowermost drug would be compressed more than the top layers. This is a valuable practical idea and does not appear to have attracted the attention which it merits.

Another neglected suggestion is that of J. W. Mill<sup>2</sup> who advised the separation of the drug into powders of various degrees of fineness,

<sup>1</sup> *Proc. A. Ph. A.* 1882, 519.

<sup>2</sup> This Journal, Vol. 43, 17, (1871).

moistening and packing separately; packing the finest drug first and the coarsest last so that the fresh menstruum should come into contact with the most difficult drug to extract. This is an early expression of the countercurrent principle now so universally used and the idea is valuable, not only for the above reason, but because a mixture of powders of all degrees of fineness from a No. 12 upwards is very difficult to exhaust satisfactorily.

#### THE ACTUAL PERCOLATION.

The actual percolation may be considered as beginning with the addition of the menstruum to the packed drug in quantity sufficient

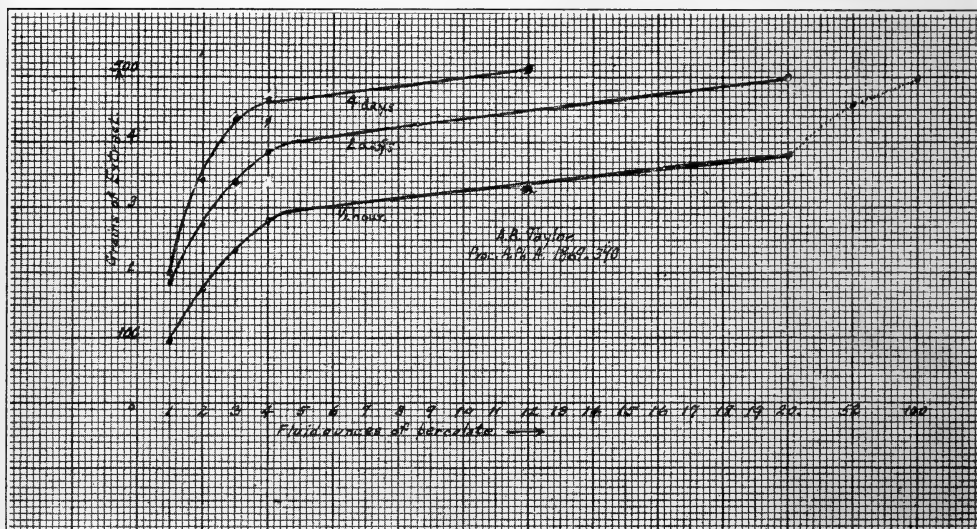


Chart A.

to fill the interstices of the drug and leave a stratum above it. To facilitate the escape of air the stopcock is usually left open until a few drops of percolate issue. The common practise at this point is to shut the stopcock and to leave the whole apparatus at rest for forty eight hours or more. This procedure, termed maceration, has been shown to be very desirable. Procter<sup>1</sup> approved of long maceration and Campbell<sup>2</sup> adopted it as one of the features of his method. Savage<sup>3</sup> showed by experiments with a long list of drugs that long macera-

<sup>1</sup> This Journal, Vol. 36, 1, (1864). *Pharm. Jour.* 19, 139, (1859).

<sup>2</sup> This Journal, Vol. 41, 384, (1869).

<sup>3</sup> *Pharm. Jour.* 24, 254, (1864).

tion produces a much more saturated first percolate. Taylor<sup>1</sup> published figures showing the effect of maceration on yellow cinchona using four troy ounces of drug and a menstruum of diluted alcohol. He macerated individual samples for one-half hour, forty-eight hours, and four days and his results are plotted in Chart. A. This shows clearly the increased concentration due to maceration and the rapidity of exhaustion after it. By two days' maceration he was able to extract as much in 20 fluidounces as were extracted in 100 fl. oz. after the half hour's maceration; and 12 fl. oz. of percolate from the four day experiment contained slightly more extract. Robbins' experiments show the same effect.<sup>2</sup> Edel also advocated lengthy maceration.<sup>3</sup> The following figures were obtained by the writer: the first drippings from the percolator were collected and analyzed, the apparatus was closed and allowed to macerate and the first 100 mls of percolate collected after the maceration was completed. Poke root gave 16.14 Gm. of dry extract per 100 mls of first drippings; after three days' maceration, 18.888 Gm. Passiflora gave 13.636 Gm. of extract per 100 mls of first drippings; after five days' maceration 15.44 Gm.

The optimum length of maceration does not seem to have been investigated. The increase in extract content is not, apparently, proportional to the time of maceration but diminishes as time proceeds. The equilibrium point would probably not be reached for weeks or even months. It becomes, then, a question of judgment to decide when the gain in extract becomes too small to justify the expenditure of time and this must be decided by each operator for himself.

At the end of the period of maceration the stopcock of the percolator is opened and the collection of the percolate begins. At this point we have in the percolator three distinct phases,<sup>4</sup> the partly exhausted drug, the absorbed menstruum, wetting the drug with whatever extractive that menstruum has dissolved, and the precolate or partly saturated menstruum distinct from that which has been absorbed by the drug. Outside the percolator we have a fourth phase, the percolate.

The absorbed menstruum may claim our immediate attention.

<sup>1</sup> *Proc. A. Ph. A.* 1869, 390.

<sup>2</sup> This Journal, Vol. 50, 329, (1878).

<sup>3</sup> *West. Drug.* 1893, 218.

<sup>4</sup> This term is not used in the physico-chemical sense.

A number of questions arise concerning it. Is it displaced by fresh menstruum? Is it constant or variable? Does it differ from the precolate? What effect does it have on percolation?

The earlier views of the percolation of plant drugs was that fresh portions of menstruum continually forced those which immediately preceded them through the mass and finally out at the bottom of the apparatus,<sup>1</sup> this being a true displacement, each layer of menstruum acting as a piston upon those layers beneath it. The Boullays therefore termed it "the method of displacement" and the term percolation did not come into general use until later.

Vauquelin<sup>2</sup> proved the displacement of salt solutions from sand by fresh water and his experiments were repeated by Deane who verified his conclusions.

Rossenwasser<sup>3</sup> appears to have been the first to challenge in print the idea of displacement. He says that cell percolation depends upon osmosis, not on displacement and offers experiments in support of his views.<sup>4</sup> Guillermond<sup>5</sup> and Soubieran<sup>6</sup> had long before shown that alcohol cannot be displaced from a marc by water without some intermixture of the two liquids.

Experiments based on the displacement of liquids from sand offer little to parallel ordinary percolation. The difference in conditions is obvious; with such "marcs" as sand there is no absorption of menstruum or solution though there may be, and probably always is, adsorption to some extent. With cellular structures there is always absorption of the menstruum, consequently there is an attracting force between the fibre and the liquid which resists the effort of the fresh menstruum to wash out the absorbed liquid. To appreciate the magnitude of this force one has only to recall the fact that huge rocks may be split by driving a wooden wedge into some crack in them and then wetting the wood. The wood absorbs the water in spite of the enormous pressure exerted against the act by the rock and, swelling in consequence, shatters the stone.

Displacement is, however, one of the factors which govern the

<sup>1</sup> The Boullays, *Jour. de. Pharm.* 21, 1, (1835). Soubieran, *This Journal*, Vol. 8, 221, (1836). Duhammel, *This Journal*, Vol. 10, 1, (1838); Deane, *Pharm. Jour.* 1, 61, (1841). Graham, *This Journal*, 31, 354, (1859).

<sup>2</sup> Quoted by Deane, (v. s.).

<sup>3</sup> *Proc. A. Ph. A.* 1882, 519.

<sup>4</sup> *Proc. A. Ph. A.* 1885, 399.

<sup>5</sup> *Jour. de. Pharm.* 21, 349, (1835).

<sup>6</sup> *This Journal*, Vol. 8, 221, (1836).

percolating of the menstruum; with the force of gravity it serves to overcome the surface tension holding liquid between the drug particles and so assists the descent of percolate.

If the process of percolation were wholly one of displacement the absorbed menstruum would present no such problem as it now does. It would simply dissolve a certain fraction of the extractive and be completely replaced by a layer of fresher menstruum, itself moving to the next lower section of drug. It is not so displaced, however, as anyone may easily conclude after watching the descent of menstruum through a moistened drug packed in a glass percolator. The new menstruum fills up the air spaces between the swollen drug particles and part of it may be absorbed if the drug was not completely saturated with liquid when it was packed. The absorbed liquid does not appear to be disturbed.

The composition of the absorbed menstruum is, of course, variable for it will contain a large amount of dissolved extractive during the early part of the process and at the end is practically pure menstruum. However, it may vary considerably from the composition of the percolate especially where the menstruum contains any large percentage of water. The marc will exert a selective absorption in such cases with the result that more water than alcohol will be absorbed by the drug.<sup>1</sup> The solvent powers of this absorbed menstruum will be different from those of the original menstruum and, consequently, the nature and quantities of the dissolved substances will not be the same in the two solutions.

I do not regard it as probable that the absorbed portions and the precolate liquid are consolute, that they freely mingle. The absorbed liquid is, for practical purposes, a solid body. It is a part of the drug being acted upon by the precolate precisely as we have been in the habit of thinking the drug was itself acted upon by the menstruum. It is much more likely that the extractive is first dissolved in the absorbed liquid whence it diffuses into the precolate which bathes each particle of drug while a further quantity of soluble matter goes into solution in the absorbed liquid. There may be some small diffusion of molecules of absorbed liquid into the precolate with concomitant replacement by molecules from the latter but this must be on so small a scale as to be negligible to all but the most minute scrutiny.

If there was a complete diffusion into the precolate or a displace-

<sup>1</sup> Cf. Patch, in discussion. *Proc. A. Ph. A.* 1892, 176.

ment of the absorbed menstruum we should find the conditions which Procter<sup>1</sup> assumed. Experimental evidence, however, disproves this contention and even in those rare cases where the second fraction of the percolate<sup>2</sup> contains more extractive than the first, an explanation may usually be found in the fact that the first portion has lain in the bottom of the percolator quite out of contact with the drug, at least in part, while the second fraction was macerating in contact with soluble material.

To the foregoing considerations may be ascribed the fact that Squibbs' repercolation process does not possess as great advantage over simple percolation as it would if we were dealing with displacement or "osmosis," and also the failures of complicated and ingenious vacuum and pressure apparatus may be due to this same cause.

Percolation does not depend upon "osmosis" except insofar as that term was used for "diffusion" by the early writers. Osmotic pressure, if it influences the process at all, serves to hinder rather than to facilitate the extraction, for it would operate to draw the menstruum into the cell instead of forcing solution out of the cell and, consequently, we should have to wait until the cells burst open from internal pressure before we could have dissolved extractive in the precolate. There is no evidence that this is the case; rather is it probable that the cell wall is so much altered in drying that it can no longer serve as a semipermeable membrane.

#### THE PRECOLATE.

The precolate is a heterogeneous mixture of solutions which fills the interstices of the packed drug from the upper layers to the stop-cock. Its composition varies by infinitesimal degrees from pure solvent to partly saturated solution. Only rarely, if ever, is any portion of the precolate a fully saturated solution; this is shown by the fact that the first portions of percolate, that is, the most concentrated portions, seldom contain as much extract as the fluidextract made from the particular drug in question.

The character of the changes in the composition of the precolate from the upper to the lowermost portions is of considerable interest from the practical as well as the theoretical point of view. Lloyd<sup>3</sup>

<sup>1</sup> This Journal, Vol. 31, 317, (1859).

<sup>2</sup> Cf. Lloyd, This Journal, Vol. 50, 438, (1878).

<sup>3</sup> *Proc. A. Ph. A.* 1881, 498; 1882, 508; 1884, 410; 1885, 411. This Journal, Vol. 80, 39, (1908).



has devoted much attention to this question especially with reference to its bearing on precipitation in fluidextracts. The writings of Squibb,<sup>1</sup> Diehl,<sup>2</sup> and others present data which bears on this problem.

As the menstruum descends through the drug it dissolves the extractive which diffuses into it and its concentration increases. With this increase in concentration its solvent powers diminish so that the rate at which it extracts soluble material from the moist drug decreases while the loss of soluble material due to adsorption becomes greater.

All solutions are subject to adsorption, for contact with a surface leads to this under the proper conditions of surface tension. Increase of surface area and of concentration in solution lead to increased adsorption. This is a factor which opposes extraction and one which intimately concerns the composition of the percolate. Out of the great variety of classes of extractible drug constituents from the water-soluble proteins to the alcohol-soluble terpenes and resins, there is present in the percolate an extremely complex and variable mixture, the components of which differ in the degree to which they are adsorbed as well as in their relative solubilities and concentrations. In such a solution slight variations of temperature and pressure as well as gain of certain constituents by solution and part loss of others through adsorption may readily upset the nicely adjusted equilibrium and lead to precipitation within the percolator. Such a condition as this would lead to striking differences in different portions of the percolate.

Again, as the percolate descends the percolator and becomes more and more saturated, two things happen; its solvent power for more of the substances already in solution diminishes while its alcoholic strength decreases. The latter fact may so alter the quality of its solvent action that there may occur a solution in quantity of substances which were but slightly dissolved out of the upper layers of the drug. In certain cases this will result in a readjustment of the solution and precipitation may result. The net effect of such an occurrence is an actual transfer of soluble materials from the upper to the lower layers of the percolator, the deposited matter being forced to wait for menstruum of proper quality before it can be redissolved and so extracted. The effect of mixing the first and last portions of percolate under such conditions is obvious.

<sup>1</sup> This Journal, Vol. 38, 109, (1866); 39, 289, 398, 513, (1867); 40, 1, (1868).

<sup>2</sup> *Proc. A. Ph. A.* 1878, 681; 1880, 424.

The rates at which the various constituents of a drug go into solution appear to differ materially; certain substances, especially those which are crystalline and of low molecular weight, diffuse more rapidly than cumbrous, amorphous compounds and so are found in larger quantity in the first portions of percolate than in later fractions. Our investigations of this most important subject have merely dipped below the surface. Squibb's work, quoted in detail below, has established the fact. In a drug like *prunus serotina* from which Power and Moore<sup>1</sup> isolated no less than fourteen constituents varying in character from a water-soluble glucoside to resin and phytosterol, the relative rates of extraction with the ordinary pharmacopoeial menstruum must be very diverse, and to this is added the possibility of the complete hydrolysis of the glucoside yielding hydrocyanic acid which, by altering the hydrogen-ion concentration of the solution, might cause precipitation of the resin.

Moreover, as the menstruum proceeds downward and the dissolving of the extractive decreases in extent, the rate of solution for any individual substance must be diminished, but there is no reason to expect that the rates of solution of all the soluble constituents are affected in the same proportion. Consequently, this is another condition which may vary the composition of the precolate.

In addition, the mutual effects of dissolved substances upon each other and upon soluble, but undissolved, material affect the composition of the precolate. Certain substances are much less soluble in solutions of some other compounds than they are in the pure solvent. Glucosides are less soluble in slightly acid liquids than they are in neutral or alkaline media. Terpene oils are quite insoluble in liquids which contain inorganic salts. Under such conditions the less soluble constituent would be obliged to remain in the marc until the greater part of the precipitant is extracted before it may be dissolved. In a case of this kind we should have qualitatively different solutions in the upper and lower regions of the percolator.

Contrariwise, many constituents of drugs are extractible by solvents in which they are really insoluble because of the presence in solution of other substances which modify their solubility. Sugars are readily extracted by alcohol although they are, as a class, but little soluble in that liquid. Glucosides which are insoluble in water may, nevertheless, often be extracted by that solvent. Gitalin,<sup>2</sup>

<sup>1</sup> *J. Chem. Soc.* 95, 243-261, (1909).

<sup>2</sup> Meyer, *Arch. exp. Path. u. Pharm.* 81, 261, 288, (1917).

from digitalis is readily soluble in chloroform but not so in water, yet owing to the presence of tannins in the leaf, it may be perfectly extracted therefrom by water but cannot be extracted by chloroform. The glucoside of oleander leaves, oleandrin,<sup>1</sup> although practically insoluble in water is readily and completely extracted by cold water owing to the modifying influence of a phenolic glucoside present which is soluble in water. Jowett<sup>2</sup> reports that emodin, though only slightly soluble in water, is extracted from cascara sagrada by an aqueous menstruum, and Squibb<sup>3</sup> stated that, while buchu could be perfectly extracted by dilute alcohol, the extract obtained by evaporating the percolate will not redissolve in dilute alcohol but requires the strong solvent. Such experiences are everyday occurrences in the manufacture of fluidextracts.

The effect of temperature on the composition of the percolate has been investigated by Norris<sup>4</sup> and Smith<sup>5</sup> who find that the percolate obtained at the higher temperature contains somewhat more extract. Smith reported that the rate of extraction of alkaloids is not greatly affected by increased temperature.

The great factor in determining the composition of the precolate is time. It is certain that, as percolation is ordinarily conducted, not enough time is allowed for equilibrium between the marc and the solution to be reached. The net effect of this is that those constituents which are quickly soluble are dissolved out while others, just as soluble but more slowly dissolved, are extracted in a fraction of their possible amount only and so are stretched through a greater volume of percolate than is necessary or desirable. The composition of the percolate will vary qualitatively according to the time it has been in contact with the drug. Several of the older writers seem to have thought a free flow of percolate desirable because they disapprove certain manipulations which "interfere with percolation" and advocate measures designed to remove impediment to rapid descent of the menstruum. I believe that such ideas are founded upon false principles; that the rate of flow of percolate is not the essential factor but that the rate of extraction is and the flow of percolate should be adjusted to yield as concentrated a liquid as the time at the

<sup>1</sup> Straub, *Arch. exp. Path. u. Pharm.* 82, 327-343, (1918).

<sup>2</sup> *Proc. A. Ph. A.* 1904, 288.

<sup>3</sup> In discussion, *Proc. A. Ph. A.* 1880, 550.

<sup>4</sup> *Proc. A. Ph. A.* 1898, 684.

<sup>5</sup> *Proc. A. Ph. A.* 1897, 245

operator's disposal will permit. Certainly, such a procedure will amply compensate in elegance and permanence of product.

(To be Continued)

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## WHO INVENTED THE TALL, NARROW PERCOLATOR?

BY GEORGE M. BERINGER, PH.M.

CAMDEN, N. J.

The historian is concerned in determining to whom credit should properly be given for each discovery, invention or advance made in our knowledge. The history of pharmaceutical products and of the apparatus and the processes used by pharmacists has not received the careful study that it merits and to determine the question of priority in the development of these will often times require critical review of the data and literature available. The longer the delay in settling questions that are involved and mooted the more difficult of settlement they become.

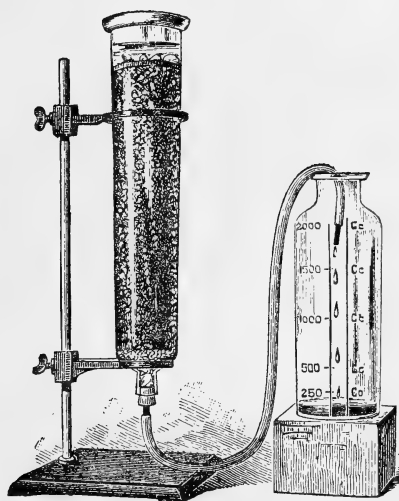
Pharmaceutical literature and the catalogues of apparatus manufacturers very generally speak of the "Oldberg" and the "Cylindrical" percolator, and credit is given to the late Prof. Oscar Oldberg for having originated this type of percolator. From the writer's study of this question he is convinced that neither the word "cylindrical" nor the appellation "Oldberg" in this connection is correct.

Reference to the original displacement apparatus of Boullay (see page 772) shows that the body or tubular portion of the percolator was really cylindrical but not proportioned in height and width to what is now accepted as the best dimensions for percolation. The orifice of the Boullay apparatus was of the funnel type with slanting sides and without the usual shoulder above the orifice of the percolator that has since been commonly adopted.

Upon referring to the original paper of Prof. Oldberg, as published in the *Proceedings* of the American Pharmaceutical Association for 1884, it is to be noted that the title thereof was "A Set of Standard Dimensions for Simple Percolators." In his paper he distinctly states that "I propose to summarize the conclusions to be derived from the able and exhaustive studies of Dr. Squibb and

Professors Diehl, Lloyd, Remington and others," and further states "there will be nothing new in the propositions here submitted." He proceeds to review the various processes of percolation, simple, re-percolation and fractional percolation.

The primary purpose of his paper, as set forth in the title, was a study of the best dimensions for simple percolators. He concludes that the " 'tall and narrow' percolators—considerably taller in proportion to their diameter than any heretofore obtainable on the



The Oldberg percolator as described in 1884.

market—are necessary to secure the proper exhaustion of the drug with a moderate quantity of menstruum, simple percolation being the process followed," and continues in the following language: "The sole object of using a tall and narrow percolator is to increase the height of the column of drug and menstruum in proportion to their mass."

After setting forth in a tabular statement the dimensions of the "standard percolators" used under his supervision in the pharmaceutical laboratory of the Chicago College of Pharmacy, he lays down as the rule for the preparation of these "that the total depth of each percolator is uniformly 5 times its large diameter and 6

times its small diameter. These percolators are, therefore, nearly cylindrical." This latter quotation proves that Dr. Oldberg himself did not apply the name "cylindrical percolator" to this type and recognized that they were not cylindrical.

It is not the writer's purpose to detract in the least from the credit due to Dr. Oldberg for formulating this rule for standard percolators of this type, nor even to intimate that he personally



The Diehl percolator as described in 1879.

was responsible for the attaching of his name to this type of percolator. However, when a critic studies, in the *Proceedings* of the American Pharmaceutical Association for 1879, the "Second Report on Fluid Extracts," by Prof. C. Lewis Diehl, he is forced to conclude that Dr. Oldberg had full knowledge of this contribution and followed in his paper the arguments advanced five years prior by Prof. Diehl.

In this communication Prof. Diehl was presenting his

study of the process of fractional percolation and whether it possessed any advantages over simple percolation properly carried out, and concluded that the object aimed at in fractional percolation could be obtained by simple percolation "if we increase the height of the column without increasing its diameter." In order to perform his experiments he states: "Being well aware, however, of the difficulties attending the percolation of high columns of vegetable powders, and particularly of narrow columns of such, I had some glass percolators constructed which, while of the same diameter at the upper and lower end as those ordinarily constructed, should be twice the usual height."

The figure illustrating his conception of a tall, narrow percolator for this purpose is reproduced herewith.

It is evident from these quotations that Dr. Oldberg followed very closely the ideas of Prof. Diehl and repeated substantially the latter's recommendations as to the approved type for percolators.

As a fact established by historical records, Diehl should be given credit in the pharmaceutical literature as the inventor of this form of percolator.

The writer is aware that, although Prof. Diehl made no published claims regarding the priority of his paper, he nevertheless felt rather keenly that credit had not been given where it was justly due. In a heretofore unpublished letter he wrote, under date of December 9, 1910:

"It does not take long to forget what has been done in previous years, and we daily discover, as new, facts which years ago have been practically demonstrated.

"How little time it takes to forget, or to overlook observations or recommendations made, is exemplified by the question of tall, narrow percolators recommended by me for preparing fluidextracts (and for extraction by percolation in general). Take a look at the percolator, Fig. 67 on p. 729 of my report in the *Proceedings* (American Pharmaceutical Association) 1879, and then compare with the percolator described and illustrated by Prof. Oldberg in the *Proceedings* 1884, pp. 388-392, which is now generally designated as the "Oldberg Percolator." Leaving the exact shape out of consideration, does not this open a question of precedence regarding the suggestion of 'tall narrow percolators;' and yet it had taken but a short five years to practically obliterate any modest claim I may have held for the suggestion made?"

## ABSTRACTS FROM THESES.\*

PRESENTED BY STUDENTS OF THE PHILADELPHIA COLLEGE OF PHARMACY AND  
SCIENCE.

## EMULSIONS OF BENZYL BENZOATE.

The extensive use of Benzyl Benzoate and its disagreeable taste has given the pharmacist an opportunity to prepare palatable forms for use by physicians.

Edwin T. Brown, in his Thesis prepared in the Pharmacy Laboratory, has shown that an emulsion is readily prepared by the use of the commonly employed emulsifying agents such as acacia and tragacanth, but that the best results followed the use of tragacanth, 2 Gm. per 100 Cc., in a 20 per cent. emulsion of benzyl benzoate.

He also tried many flavors, including varying proportions of aromatic elixir of eriodictyon, "aromol," 10 and 20 drops per 100 Cc.; methyl salicylate and oil of cinnamon, each 12 drops per 100 Cc.; oil of cinnamon, 12 drops, methyl salicylate 18 drops per 100 Cc. of emulsion; methyl salicylate, 10 drops, oil of sassafras, 8 drops, and oil of sweet orange 12 drops per 100 mls; 12 drops each of the same three oils and 8 grains of vanillin per 100 Cc. of emulsion.

The conclusion reached by Mr. Brown is that 20 drops of "aromol" or 12 drops each of methyl salicylate, oil of sassafras and sweet orange are the best flavors tried, although even these large amounts of aromatics fail to completely cover the disagreeable taste of the benzyl benzoate.

## NOTES ON THE ASSAY OF PHOSPHORIC ACID.

The U. S. P. IX assay for phosphoric acid has proven unsatisfactory in the hands of many chemists. This assay is inconsistent in its conclusions, and therefore inaccurate because of the varying amounts of zinc oxide, which may be added, and which make up a part of the final volume from which an aliquot portion is taken for titration.

Mr. H. L. Cline in a thesis prepared in the Chemical Laboratory proposes to overcome this difficulty by filtering the liquid, after neutralization with zinc oxide (using a Gooch crucible) washing the precipitate with water until free from silver nitrate and adding distilled water to make the total volume measure exactly 100 mls. An aliquot portion of this solution is then titrated with tenth-normal

\* Prepared by E. Fullerton Cook, Ph.M. and A. B. Nichols, Phar.D.



potassium sulphocyanate solution in the usual manner, and calculated from the per cent. of phosphoric acid.

By eliminating the variable factor, the zinc oxide, concordant results have been obtained in a number of assays in the hands of different operators.

#### MODIFIED METHOD FOR PREPARING ETHYL NITRATE.

In a thesis prepared in the Pharmacy Laboratory, Charles H. Pitt states the use of a separatory funnel for the collection of ethyl nitrite as it floats upon the surface of the saturated sodium sulphate solution, as directed by the U. S. P. IX, has not proven satisfactory in the hands of many operators. The chief objection is the large loss from evaporation during the process. To overcome this, where the distillation method is not available, Mr. Pitt has devised an apparatus which largely prevents loss from evaporation. He proceeds as follows:

Two large flasks are placed in ice-baths, and the one closed by a doubly perforated stopper. Through one perforation a thistle tube (or a glass tube connected at the top by a piece of rubber hose with a small funnel) is inserted, so that it extends almost to the bottom of the flask. A second tube, bent at a right angle an inch above the stopper is inserted in the other perforation and just passed through the stopper. This tube is again bent at a right angle and the outlet end inserted in the second flask, extending almost to the bottom.

The reaction between the sodium nitrite, alcohol, and sulphuric acid is now carried on as usual, in the cold first flask, and when the strata of ethyl nitrite has collected on the surface of the mixture in the flask, more water is carefully poured in, through the funnel tube, until it forces the ethyl nitrite over into the second flask, through the connecting tube. Now the tubes are reversed, and the washing with sodium carbonate solution accomplished in the second flask the ethyl nitrite being subsequently returned to the first flask by adding water as before, the first flask having, of course, been cleaned. It is now washed with cold water as before, and, when finally treated with potassium carbonate is ready for dilution with alcohol for the preparation of the spirit.

Distillation flasks, with a side tube, may to advantage replace the usual Florentine or Erlenmeyer flasks whereby the contact with a rubber stopper is avoided.

By this method practically all loss by evaporation is avoided

and the preparation of ethyl nitrite made possible with very simple apparatus.

#### FREQUENTLY USED SATURATED SOLUTIONS.

The dispensing pharmacist is frequently called upon to prepare saturated solutions of certain salts, and is accustomed to depend upon the solubility statements of the Pharmacopoeia as a guide. These figures are valuable so far as the information goes, but do not show the volume of the completed solution, and therefore are an incomplete guide where a definite volume of a saturated solution is to be prepared.

Lewis G. Freeman in a thesis prepared in the Pharmacy Laboratory has undertaken experiments to supply these desired figures for several salts often called for in the form of saturated solutions. In each instance a definite weight of strictly U. S. P. salt was taken (10 Gm.) and the solubility checked in three ways. First the exact amount required for solutions, as stated by the U. S. P., was added, the mixture frequently agitated at 25° C., in a tube, graduated to tenths of a Cc., until solution resulted. It was necessary in all cases to add slightly more water, to dissolve the salt than stated by the Pharmacopoeia. When completely dissolved, the final volume was noted.

By the second method the salt (10 Gm.) was dissolved in the specified volume of water, with the aid of heat, but a slight additional amount of water was required to prevent crystallization on cooling. Again the volume was noted.

In the third experiment an excess of the salt was agitated with distilled water, at 25° C., until the solution was saturated, the mixture filtered, and a definite volume (10 Cc.) carefully evaporated. The weight of the salt obtained was then calculated for a comparative basis. The average of these figures was used in the following results.

The figures showing the amount of salt and water to take for making 100 Cc. 1 fluidounce, and 16 fluidounces of a saturated solution are calculated from the experiment with 10 Gm. of salt.

#### Potassium Iodide.

KI taken, 10 Gm. . . . .	99 (98.52) Gm.	451 (450.47) Grs.	1 Lb. av. 208 Gr.
Water taken, 7.2 Cc. . . . .	71 (70.93) Cc.	340 (340.39) Min.	11 Fl. Oz. 166 Min.
Resulting volume,			
10.15 Cc. . . . .	100 Cc.	1 Fl. Oz.	16 Fl. Oz.

Sodium Iodide.

NaI taken, 10 Gm...	110 (110.13) Gm.	502 (502.4) Gr.	18 Oz. av. 163 Gr.
Water taken, 5.5 Cc.	61 (60.57) Cc.	291 (290.68) Min.	9 Fl. Oz. 331 Min.
Resulting volume,			
9.08 Cc.....	100 Cc.	1 Fl. Oz.	16 Fl. Oz.

Magnesium Sulphate.

MgSO <sub>4</sub> taken, 10 Gm.	63 (62.9) Gm.	287 (286.99) Gr.	10 Oz. av. 217 Gr.
Water taken, 10 Cc..	63 (62.9) Cc.	302 (301.87) Min.	10 Fl. Oz. 30 Min.
Resulting volume,			
15.9 Cc.....	100 Cc.	1 Fl. Oz.	16 Fl. Oz.

## BACTERIA IN (SO CALLED) SOFT DRINKS.

LOUIS GERSHENFELD, PH.M., B.Sc.,

PHILADELPHIA, PA.

Scientific investigation has given ample proof that there is a close connection between the spread of disease and the water that is used in a community. A pure water supply is of first importance in the prevention of disease and in the conservation of public health.

From time to time, there has been considerable discussion over the superiority of the chemical or bacteriological examination of water. This has been quite useless, for though a bacteriological analysis may be shown to be of greater importance, a chemical examination will nevertheless detect the presence of certain chemical substances, from the relative amounts of which, an inference may be drawn as to the existence of pollution with human or animal excreta, or, in some instances, with poisonous or injurious compounds. It is therefore apparent that both examinations should be carried out.

It is with this in mind, that communities are compelled either by state or other recognized authority, to determine the purity of their water supplies, by performing bacteriological and chemical examinations at frequent intervals.

It is, of course, evident that such steps taken for the careful guarding of our water supplies are justifiable. Furthermore, it is apparent why sanitarians soon became interested in the control of milk, cream, ice cream, ketchup and other food supplies, so as to determine that these products will not introduce disease into the numerous communities. But there seems to be one class, the soft drinks, used so extensively, that has been sadly neglected by the

sanitarian. In fact many use soft drinks, bottled or otherwise, almost exclusively for drinking, while the potable water supplied is used for every purpose other than drinking.

The writer is aware that some municipalities attempt to guard the market supply of soft drinks in behalf of the health of their respective communities, but he is assured that effort along these lines is indeed small. There is no doubt that no other product is supplied to the public in such large quantities, as are soft drinks.

A *pure* soft drink is just as essential to the prevention of disease as is potable water, milk, etc. At present, many behind the pure food movement, carefully investigate these products, to be assured that saccharine or an injurious coal tar coloring preparation is not being used. A chemical examination to indicate pollution with animal excreta is not warranted or necessary, due to the fact that a potable and chemically pure water is furnished to the plant for the manufacture of the numerous products and the finished preparation does not stay around long enough to show any apparent ageing or decomposition.

The chemical methods of examining soft drink supplies, as previously mentioned, will not detect the presence of bacteria, much less assist in their identification. A bacteriological examination of such water will, however, reveal the number and in some instances the types of bacteria in a given volume. The fact should not be overlooked that even though a potable water was used, the finished product may nevertheless be highly contaminated, due to the carelessness and unsanitary methods used in the manufacture of the preparation.

The bacteriological examination of soft drinks is a more direct and delicate test, both as to the sanitary operation of the plant, as well as on the factors, that have an important bearing as to the value of the finished product. An analysis of the bacterial content of a soft drink will quickly reveal the hygienic conditions, prevailing at the time of the manufacture of the particular preparation. Early examinations may prevent epidemics, as they act as a check. It would be advisable to make an inspection of the plant, to determine the cause of the pollution, and to advise the remedial measures to correct any evil that may exist.

It has been the privilege of the writer to guard from a sanitary standpoint the making of soft drinks, and it is for this reason that he advises all manufacturers, not only of soft drinks but of all bottled

water to protect themselves, by carefully supervising the manufacture as well as the finished preparations. It is advisable that they start early to control the bacterial content of their samples, before they will be compelled to do so, as there is no doubt that in the near future, legal requirements will necessitate such supervision.

A community has a right to demand that whatever qualities soft drinks may claim or may possess, these should be secondary to cleanliness and it should be the duty of those who guard the health of the community to determine whether such products are free from contamination. The public should demand this as they have the right to expect it. Many laymen are under the impression that such strict supervision is at present being exercised by proper authorities.

The water used in the manufacture of the soft drinks in plants, under the writer's observation, was usually found to be potable. The danger of contamination is due more to the careless washing of the containers, or the introduction of a contaminated flavoring syrup, or to minor details carried out during the operation. Actual inspection of the plant during every stage of manufacture, together with bacteriological examinations of all ingredients entering into the preparation of the beverage will lead to a determination of the responsibility for any unsuitable product. In the long run, such inspections and examinations save untold worry and considerable expense.

An artificially carbonated water prepared under cleanly conditions, will usually show a low bacterial content. The writer carbonated a number of samples on one occasion. The containers were cleansed properly, the flavoring syrup was low in bacteria, and all other procedures were guarded as they should be by any one familiar with the simple technique of filling the bottles. The bacterial content of the finished preparation was lower Cc. per Cc. than was observed in the water used in preparing the product.

To actually show what the condition is, the writer obtained 15 samples of different brands of soft drinks. Many of these were bought during the months of April and early May, and obtained from lots that were delivered, in most instances, in his presence. He was thus assured, that the samples represented the finished products as sent out from the plants of the various manufacturers and did not represent samples that were allowed to incubate at room temperature or exposed to heat in the retail stores.

Of the fifteen samples, six, or 40 per cent., were found to contain

*B. Coli* in 10 Cc. portions. Lactose Bile and Lactose Bouillon were used for the presumptive test for *B. Coli*. Three 10 Cc. portions were used. In all of the six reported instances, *B. Coli* were isolated from the fermentation tubes.

One gave considerable gas with all three 10 Cc. portions. No *B. Coli* were found, but *B. Welchii*, another sewage bacterium, was present.

In the total bacterial counts on agar at 37° C. after 48 hrs. incubation, two showed counts lower than 100 per Cc. Three samples showed the presence of less than 300 bacteria per Cc. Three others had a bacterial content ranging between 500 and 1000 per Cc. The other 7 had a count of over 1000 bacteria per Cc. The bacterial count on agar at 20° C. in most all of the foregoing samples was somewhat higher than the 37° C. counts.

Some of the organisms found were staphylococci; short and long, chain streptococci; *B. Coli*; *B. Welchii*; *B. Cloacae*; *B. Subtilis*; *B. Mycoides*; *B. Mesentericus Vulgatus*; diphtheroids; streptothrices and molds.

The occurrence of some of the foregoing does not speak well as to the cleanliness of the samples or of the desirability of indulging constantly in such drinks.

Facts such as these give weight to the opinion, entertained by the writer, that more attention must be given to the sanitary aspect of this whole problem.

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#### THE PROFESSOR—AS YET UNSTANDARDIZED.\*

BY J. W. STURMER, PHAR. D.,  
PHILADELPHIA, PA.

According to Garfield, Dr. Hopkins seated on a log, constituted an institution of higher learning adequately equipped to afford a liberal education to the student fortunate enough to occupy a seat on the same log with this learned doctor.

Higher education has developed marvelously since Garfield coined his famous phrase in laudation of Dr. Hopkins. The log is now represented by pretentious buildings, with commodious lecture rooms, excellent laboratories, well-stocked libraries, and the various appurtenances and aids, such as projection apparatus, charts, etc., which the modern instructor finds helpful in transmitting

\* Read at the Washington meeting of the American Conference of Pharmaceutical Faculties, May, 1920.

knowledge to his more or less receptive students. Millions have been invested and invested to good purpose in physical equipment for education. So important is this equipment deemed that this Conference has seen fit to fix a minimum standard in this respect for the schools and colleges of pharmacy which constitute its membership. And who would contend that this standard which the Conference has set, is without value?

But educational bodies including the Conference have gone further. They have in a way standardized the student—at least they have set up certain entrance requirements to ensure, on his part, a proper preparation for his college work. This also was good common sense and made for real progress in pharmaceutical education.

The evolution of the log having eventuated so splendidly and the matter of entrance requirements being definitely settled there are those who now make inquiry why this very conspicuous educational advancement has not brought results which are commensurate with the progress made. We may answer and furnish evidence to substantiate our statement that there has been in very fact a considerable gain. Not that the best men of our present classes are necessarily better than the best men of the past—but the average is better and the poorest of the present-day graduates show a marked improvement over the poorest of the earlier classes. Despite this distinct gain there is, to be sure, still much room for improvement in our schools of pharmacy. We are convinced, however, that the next conspicuous advance in the schools of this Conference will not result primarily from further elaboration of material equipment, nor will it be due to the adoption of still higher entrance requirements; it will result rather from improvements in the curricula and in the development of higher efficiency in the art of teaching. After all, the professor is the all-important factor in the educational mechanism. His personality will compensate for a lack in teaching facilities; his inefficiency can render almost worthless the finest equipment.

The particular service of this Conference has in the past been largely in the matter of fixing standards—standards for equipment, standards for entrance requirements, standards for the faculties from the standpoint of numerical strength. And when we proceed to take up seriously the most complicated educational problem of all, namely the professor, the first step suggested will no doubt be the establishing of standards with reference to his academic titles,

and it will be decreed that a professor shall possess certain scholastic qualifications. That such standards are both feasible and useful is evidenced by the fact that requirements as to degrees attained have for years formed a part of the policy of many educational institutions in the matter of selecting new members for their faculties.

But it must be remembered that while the basic principle underlying such a policy is sound enough, scholastic standards by themselves cannot ensure an efficient faculty, for the proud possessor of a doctorate, notwithstanding the etymology of the word, is not necessarily a teacher and may in fact never, because of certain unfavorable character traits, develop into a good teacher. Nor can we be sure that the promising young post-graduate who has planned and has executed a creditable piece of research has thereby proven his ability to teach classes. Indeed, research ability precious as it is and necessary for the advancement of science, may be possessed by a person wholly unfitted temperamentally to deal successfully with students. Sometimes, to be sure, we find high research ability and the essential qualifications of a teacher in the same person. But it is but seldom that nature so lavishly endows one of its children.

Having disposed of the relatively simple matter of academic standards for the professor, the Conference may next investigate his ability as a teacher. Has he the power of clear exposition—the ability to develop his subject in a logical manner? Has he mastered the technique of lecture demonstrations? Does he know—and does he proceed on the basis of such knowledge—that if experiments are not properly timed, or if the point to be demonstrated is obscured by over-emphasis of certain details, the student is confused rather than helped by this accessory to the lecture? Does he perpetrate that most serious yet common fault of using technical terms unfamiliar to the student or does he avoid such terms until they can be explained with proper connections so that the student's mastery of the nomenclature may develop with his progress in the science? Alas, who has not heard a biology lecture which seemed to be in a foreign language, and wondered how there can be so much verbiage about so little foliage. Can he capitalize his sense of humor and give human interest to his subject without falling into a hopeless condition of anecdotage which renders him ludicrous rather than humorous. We learn to teach by constant trial and by observing the methods of our elders—in this way rather than by following rules and precepts. But does our young professor know that the success-



ful teacher has not only developed methods which are inherently and intrinsically good but has also attuned them to his own personality?—or has he fallen into the error of slavish imitation? Is he a mere automatic transmitter of knowledge, or has he a spark of that marvelous fire which inspires others to become willing and productive workers in the field? For this is after all the most essential qualification of a good teacher.

If we look back over the list of teachers with whom we have been in personal contact, we are rather surprised to find that those who have scored the most pronounced success are not necessarily the most erudite of the lists nor the most productive investigators nor even the men employing the most approved pedagogic methods, but those inspirational personalities who imparted to their students their own enthusiasm and their own love for the work. If the results of teaching are to be measured by the productive workers produced rather than by the number of correct answers the students can give in the final examination—and this is the real criterion—it is the inspirational teacher who must be accorded the highest place in the teachers' hall of fame. And let us remember, that no teacher can inspire his students unless he is convinced of the deep and lasting importance of his subject.

Pharmacy in particular has suffered severely at the hands of its iconoclastic friends and its apostles of negations—who contend that medicine is the science of diagnosing disease—that cures are impossible—that therapeutics teaches the futility of drug medication—that vegetable histology deals with intercellular air spaces—that pharmacy is a collection of cook-book recipes for the preparation of useless concoctions. Let us remember that we cannot kindle the enthusiasm of our students with epigrammatic negations. Unless the professor of a pharmacy school believes in pharmacy as a necessary and important part of the world's work, his influence will be positively harmful. So we can rightfully ask also does the professor who has met our other requirements also, meet this: does he subscribe to the articles of faith of true pharmacy? Does he firmly believe that he is training his students to become useful citizens who will earn their daily bread in the service of their fellow men?

In standardizing the professor, let us attack the problem as a complicated one involving the human equation. Let us not be too mathematical, too mechanical. Let us not overlook the potential Dr. Hopkins and accept the mere bookworm.

Let us deal with the professor in a broad and sympathetic way. He is the all-important factor in our educational scheme which we have so laboriously builded. With him rests largely the future of pharmacy, for it is he who deals with the on-coming generation of pharmacists. Let us standardize the professor by all means; but let us do it wisely.

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## THE EFFECTS OF PROLONGED HEATING AND OF AQUEOUS EXTRACTION ON OPIUM.

BY ALEX. M. MACMILLAN AND ALFRED TINGLE,

OTTAWA, ONT., CANADA.

### INTRODUCTION.

The work of H. A. Annett and Hardayal Singh<sup>1</sup> on the change of morphine content produced by heating opium was of such interest to the Customs and Inland Revenue Laboratory at Ottawa that it was found desirable to check the results and endeavor to confirm them. We also wished to extend the scope of the observations recorded and we believed that we could improve on some points of procedure, eliminating or minimizing certain possible sources of error.

Our conclusions differ from those of these previous authors. We cannot consider that the variations in experimental conditions are wholly responsible for the different results obtained. We should have preferred to carry our work much further, so that it might be final rather than tentative. Both of us having left the laboratory where we undertook this investigation, and neither of us being in a position to continue it alone, we have decided that it is best to publish these results as they stand, leaving the last word on the subject to some other worker.

H. A. Annett and Hardayal Singh used the B. P. method for their estimations of morphine. While as good as any method then available, it is open to three objections: (1) The results admittedly may vary as much as 0.5 per cent. in either direction. (2) Its adoption made it necessary to add enough water to the heated material to bring it back to its original weight. Justification for such action

<sup>1</sup> *Jour. Soc. Chem. Ind.*, 37: 315T, 1918.

rests on the unproved assumption that the observed loss of weight is entirely due to loss of moisture pre-existing in the opium. (3) The published discussion on their paper<sup>1</sup> shows that it is doubtful whether the B. P. method has the same degree of accuracy for heated as for unheated opium.

We believe that we have overcome these objections in our own work by using the method of estimating morphine devised by one of us (T)<sup>2</sup> which is equally applicable to opium in any form irrespective of previous heating, and regardless of its moisture content for which no "correction" is necessary.

The claim has already been frequently made that water alone, even when boiling, will not extract all the morphine from opium<sup>3</sup> and that an aqueous extract of opium loses morphine when boiled or evaporated on the water bath. With the material at hand we intended to enquire further into these matters. Our actual results do not go very far for the reason already mentioned, but at least confirm those of previous workers.

#### EXPERIMENTAL.

*The Effect of Prolonged Heating on Opium.*—Each batch of opium was prepared by being air-dried, powdered in a glass mortar, and passed through a 40-mesh sieve. The resulting powder was heated at 60° C. for 24 hours, then transferred to a can with a tight (but probably not air-tight) lid in which it remained till the working samples were withdrawn. These were all taken at the same time each consisting of 6 Gms. weighed on balanced watch glasses. Those which were not to be immediately analyzed to establish the morphine content of the material before heat treatment were placed in a Frea's electric oven (at atmospheric pressure) heated at 98°–100°. These heated samples were re-weighed at intervals and at predetermined times samples were withdrawn from further heating, the morphine content then being determined by the method already mentioned. Two batches of opium were experimented upon, one being of Persian the other of Indian origin. The results are tabulated below.

<sup>1</sup> *Loc. cit.*

<sup>2</sup> *Amer. Jour. Pharm.*, 90: 851, 1918.

<sup>3</sup> Debourdeaux, *Bull. Sci. Pharm.*, 17: 382, 1910.

TABLE I.—THE EFFECT OF HEAT ON PERSIAN OPIUM AS TO WEIGHT AND MORPHINE CONTENT. ASSAY OF AN UNHEATED SAMPLE SHOWED MORPHINE 9.35%.

Time of Heating (Hours).	Weight of Opium after Heating (Grams).		Weight Lost by Opium (Per Cent.).	
	Sample No. 1.	Sample No. 2.	Sample No. 1.	Sample No. 2.
0	6.0000	6.0000	....	....
24	5.8112	5.8005	3.14	3.32
48	5.7668	5.7596	3.89	4.00
72	5.7410	5.7460	4.31	4.23
96	5.7260	5.7174	4.57	4.71
192	.....	5.6674	....	5.54
288	.....	5.6360	....	6.07
Percentage of morphine found at end of heating.			5.98	5.98

TABLE II.—THE EFFECT OF HEAT ON INDIAN OPIUM AS TO WEIGHT AND MORPHINE CONTENT. ASSAY OF TWO UNHEATED SAMPLES SHOWED MORPHINE 6.56% AND 6.66%.

Time of Heating (Hours).	Weight of Opium after Heating (Grams).					Weight Lost by Opium (Per Cent.).				
	Sample No. 3.	Sample No. 4.	Sample No. 5.	Sample No. 6.	Sample No. 7.	Sample No. 3.	Sample No. 4.	Sample No. 5.	Sample No. 6.	Sample No. 7.
0	6.0000	6.0000	6.0000	6.0000	6.0000	....	....	....	....	....
24	5.8243	5.8355	5.8892	5.8846	5.8835	2.93	2.74	1.84	1.92	1.94
48	5.8138	5.8215	5.8257	5.8236	5.8012	3.10	2.97	2.90	2.94	3.31
72	5.7843	5.7775	5.8107	5.8076	5.7967	3.59	3.71	3.15	3.20	3.39
96	5.7748	5.7665	5.7592	5.7801	5.5527	3.75	3.81	4.01	3.66	4.12
192	5.7143	5.7235	5.7087	5.7256	5.7057	4.76	4.61	4.85	4.57	4.90
288	.....	5.7020	5.6892	5.6961	5.6797	....	4.97	5.18	5.06	5.34
384	.....	.....	5.6747	5.6651	5.6657	....	....	5.42	5.58	5.74
480	.....	.....	.....	5.6531	5.6402	....	....	....	5.78	5.99
576	.....	.....	.....	.....	5.6277	....	....	....	....	6.20
Percentage of morphine found at end of heating						6.40	5.64	5.54	5.13	4.52

*The Effect of Prolonged Heating on Crystallized Morphine.*—While it has no necessary bearing on the changes undergone by such a product as opium, we believed there would be some collateral interest in making a careful measurement of any alteration which morphine might undergo when heated. From a specimen of very pure crystallized morphine 1 gram was exactly weighed on a balanced watch glass. It was then heated in the electric oven between 98° and 100° C. and weighed at intervals.

Time of Heating (Hours).	Weight of Sample (Grams).	Total Loss of Weight (Grams).
24	0.9406	0.0594
48	0.9406	0.0594
72	0.9406	0.0594
96	0.9407	0.0593
192	0.9408	0.0592

The loss of 0.0594 corresponds exactly to the weight of the theoretical water of crystallization. After being heated for 96 hours a yellow tinge was observed in the previously white powder. This became decidedly deeper when the heating had been prolonged for 192 hours.

*The Extraction of Morphine from Opium by Hot Water.*—An experiment was made on the Persian opium previously used, to show (1) how much morphine would remain undissolved by hot water and (2) how much morphine would be destroyed under the conditions of extraction.

A sample weighing 6 grams was extracted with hot water in a Soxhlet Extractor till the overflowing liquid showed no further color. This involved boiling for about 16 hours. The exhausted residue was carefully collected and dried first in the air then in a desiccator. Determinations of morphine were then made on the whole both of the exhausted residue and of the extract.

	Total Weight of Morphine Found (Grams).	Percentage of Morphine on Original Weight of Opium.
In exhausted residue.....	0.0100	0.17
In concentrated aqueous extract.....	0.4965	8.27
Morphine lost (by difference).....	0.0545	0.91
Total.....	0.5610	9.35
Found by assay of original opium.....	0.5610	9.35

#### DISCUSSION OF RESULTS.

*Loss of Weight by Opium When Heated.*—Our results show a steady loss of weight when opium is heated. There is no sign of constancy having been attained even after 576 hours at 98°–100° C. Different samples agreed very fairly among themselves considering that the material was weighed on open watch glasses and is always somewhat hygroscopic. On these points we are at variance with Annett and Hardayal Singh,<sup>1</sup> who claim to have obtained

<sup>1</sup> *Loc. cit.*

practically constant weights after 192 hours. Our Sample No. 7 (Table II) shows a loss of more than 1 per cent. in the period 192 to 576 hours. These workers also assert that opium is practically non-hygroscopic when dried at about  $100^{\circ}$ . On this minor point also our results are not parallel. As would be expected, we are able to agree that the greatest loss of weight takes place in the first or second day of heating.

*Change in the Morphine Content of Opium When Heated.*—Our results point to a sharp difference between Persian and Indian opium. Table I shows that the Persian opium lost more than 30 per cent. of its morphine on being heated for 96 hours, but lost no more when the heating was continued to 288 hours. On the other hand Table II shows the Indian opium as having lost only about 3 per cent. of its morphine on being heated for 192 hours, but as losing progressively and heavily till it had lost about 30 per cent. on 576 hours' heating. Again we differ from Annett and Hardayal Singh, who claim to have found an increase in the morphine content from 264 hours to 288 hours' heating, though we agree with them (as regards Indian opium on which alone they worked) that the first period of heating causes no great change but that once started it proceeds regularly up to 264 hours. None of their experiments cover a longer period than 288 hours. It seems probable that the slight rise in morphine-content which they report is due solely to an analytical error. Their results differ markedly from those we have obtained on Persian opium.

Our conclusion is that many more comparative experiments are necessary before it can be definitely stated that Indian and Persian opium differ in their behavior towards heat. We consider it as proved, however, that some samples of opium lose a notable amount of morphine before all the moisture has been expelled. We believe that while further investigation is called for, it would be well to take into consideration the facts already shown in planning any assay of opium.

*The Effect of Prolonged Heating on Crystallized Morphine.*—The free alkaloid proved to be much more stable than we anticipated. While it lost its water of crystallization during the first day of heating, no further change could be detected till it had been heated for four days. Even when heated for eight days it had only gained 0.2 Mg. over its anhydrous weight and any change in its basicity was not appreciable. After such a period of heating opium, itself, had shown a decided destruction of morphine salts.

*The Extraction of Opium by Hot Water.*—Our single experiment on this point illustrates once more what has been previously shown by others, *viz.*, that water alone does not completely extract morphine compounds from opium. In our sample we found 0.17 per cent. of morphine (nearly 2 per cent. of the total originally present) was not extracted even under somewhat drastic treatment. We also found that the destruction of morphine by prolonged digestion of the extract was 0.91 per cent. (more than 9 per cent. of the total originally present). While these points are not new, it appears to us that they call for more notice than they have yet obtained seeing that they have bearing both on some methods of assaying opium and on the preparation of certain pharmaceutical products.

This work was planned and carried out by us in the Analytical Laboratory of the Department of Customs and Inland Revenue, Ottawa, Canada. We wish to extend our thanks to Mr. F. W. Babington the head of that Laboratory for many acts of kindness which gave us time and opportunity to do more than the routine work which was necessarily our chief concern.

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## THE MULFORD BIOLOGICAL EXPLORATION OF THE AMAZON BASIN.

Preliminary and more or less erroneous announcements of this enterprise have appeared in the daily press, but without details as to the objects of the work and its special relations to medicine and pharmacy. The following is a complete prospectus of the Exploration.

The original idea of the expedition was far less comprehensive than that which now has developed. Doctor Rusby having gained information from travelers in northwestern Brazil of certain medicines in use by the natives which possessed very interesting properties, and properties that might render them of value in medicine, has long desired to observe their effects as there used, and to secure supplies for scientific investigation, and it was to carry out this object that the plan was originally conceived. In performing this work it would also be practicable to make a general collection of the flora of a very extensive region in southeastern Colombia and northwestern Brazil, in which no botanical collections have as yet been made. Since the New York Botanical Garden, Harvard

University and the National Museum have recently undertaken to prepare a flora of northern South America, including the region referred to, this added work would be most timely. Additional interest attached to such collecting because it would go far toward completing the survey of the Andean flora on which Dr. Rusby has done so much in his travels in Chile, Bolivia, Colombia, Brazil and Venezuela. Dr. Rusby is, moreover, Honorary Curator of the Economic Museum of the New York Botanical Garden, of which an elaborate catalogue is now going through the press. In the performance of this work he has been impressed with the long list of economic products of the region in question of which no authentic museum specimens exist. Many of the drugs of the region are very imperfectly known, as to their origin and collection. In the same connection, the Doctor was desirous of visiting southeastern Bolivia, the only part of that country where he has not made collections. With all these objects in view, Dr. Rusby appealed to the H. K. Mulford Company for coöperation in the carrying out of such an undertaking. Mr. Milton Campbell, the President, submitted the idea to his scientific department, with the result of considerably extending the scope of the work. It was pointed out that a number of the endemic diseases of the tropics were very imperfectly known, and that their careful study would not only prove of scientific value, but might result in the discovery of curative measures. It was particularly desirable that the transmission of diseases by insect agency should be thoroughly investigated. A discussion of these subjects showing that their investigation was feasible, the proposition was submitted to the Directors of the Mulford Company and was approved. Dr. Rusby's original plan, as submitted to Mr. Campbell, had included provisions for commercial adjuncts by which the expenses of the exploration would be repaid and a probable profit returned, but the Mulford Company deleted these items, stating that they preferred public recognition as making a contribution to science and to medicine, free from all direct commercial returns.

The subject of entomology having thus been included in the research, it was decided to broaden this work and to make a general collection of insects, and arrangements were made with the United States Bureau of Entomology to classify these insects and report upon them. Out of these discussions a suggestion arose for studying methods of repelling or destroying the numerous tropical insects which so annoy travelers and not infrequently become the indirect



causes of fatalities, and officers of the Federal Insecticide and Fungicide Board prepared a comprehensive series of formulae of substances that might prove useful in this direction. Supplies of these mixtures will be taken and systematically tested. At the same time, every opportunity will be improved for recording the pollination of flowers by particular insects and those destructive to timber and other vegetation will be studied. It is hoped that the Bureau of Entomology may detail one of its representatives to accompany the party.

Dr. Rusby had been greatly interested, on previous expeditions, in the immense variety of fishes in the Amazon basin, and in the peculiar characters and habits of many of them, and determined to carry materials for extensive collections of this fauna. On submitting this idea to Drs. David Starr Jordan, and C. H. Eigenmann, among the leading authorities on the subject, they at once expressed their readiness to assist in the investigation of the fishes collected. It is also probable that they will be represented upon the Exploration by one of the ichthyologists from the University of Indiana.

Among other subjects of interest, is that of oil-seeds, of which there is a vast variety in the forests of tropical America. From fifty to a hundred pounds or more of each of these will be collected as encountered, and these will be shipped home for expression and the study of their oils. Professor Augustus A. Gill, of the Boston Institute of Technology has undertaken to pursue these researches. Similarly there are very many plants containing essential oils that are likely to prove of value, and Dr. Edward Kremers, of the University of Wisconsin will interest himself in the study of these. The region to be traversed abounds in serpents and other reptiles, both poisonous and innocent. These will be preserved like the fishes. The batrachians will be sent to Professor Ruthven, of the University of Michigan, and the others to the American Museum of Natural History in New York City.

While all these subjects are of great interest, the special work of Dr. Rusby and his party will be in connection with medicinal plants and drugs, for the study of which elaborate provisions have been made. Dr. Rusby hopes to shed fresh light on the manufacture of blow gun and other arrow poisons, of which several varieties appear to be in use in the region to be visited. Some of the more important commercial drugs will be traced to their origin, and absolutely authentic material will be secured for study. A very

superior quality of rubber is produced in the region and this will receive close attention. No opportunity will be lost for securing materials from which the nature of tropical diseases can be studied in the Mulford Laboratories at Glenolden.

The complete study of the medicinal products will occupy the attention of many specialists. Dr. Rusby will himself undertake their botanical classification and description. Their microscopical study will be pursued by Dr. Ballard at the Columbia University School of Pharmacy, by Professor Younken at Philadelphia, Schneider of Nebraska, Newcomb of Minnesota and others. Their chemistry will be studied by Army of Columbia, Jordan of Purdue, Sayre and Havenhill of Kansas. The study of their physiological and medicinal properties will occupy the attention of many medical men at Yale, Harvard, the University of Pennsylvania, Johns Hopkins, and connected with the American Medical Association headquarters in Chicago.

The Division of Biology and Agriculture of the National Research Council has interested itself actively in this enterprise and has rendered valuable assistance.

The general route to be traversed by the party will be the country along the base of the Andes from Villavicensio, southeast of Bogota, to Calamar, several hundred miles south. At various points the valleys and canons issuing from the mountains will be ascended and collections made. A number of lakes along the route will also be visited. At Calamar, land travel will be abandoned and river-boats secured for the descent of the Uaupes River. Until a recent period, only the lower part of this river was known to science. There are a number of rubber collecting stations along its course, and it has been more or less traversed by traders. For the most part, however, this region is occupied by little or not at all civilized aborigines, who at times at least have exhibited hostility against the whites. For our knowledge of this region, science is almost wholly indebted to the work of Dr. Hamilton Rice, who, in the face of great difficulties, and under great hardships, traversed the river almost from its source to its mouth at the Rio Negro. Dr. Rice has given us two excellent and comprehensive accounts of it, in the *Geographical Journal* for June, 1910 and August, 1914. Both papers are accompanied by maps, not only of this, but of neighboring rivers which he first explored.

Judged by its peculiar position and topography, the section to

be studied must be very rich in its variety of both plants and animals. It is probable, moreover, that its paleontological records are of great interest. Into this field of collection, however, the party cannot enter, because of the time required for the collection of fossils and the weight of the specimens.

On reaching the Rio Negro, the party will descend to its mouth at the Amazon, which they expect to reach early in July, thus avoiding the rainy season north of the Amazon. At this time the dry season will begin south of the Amazon, and the party will then commence the ascent of the Madeira, the largest southern tributary of the Amazon. Steamers run direct from Manaus on the Amazon, to the lowest cataract of the Madeira. From there a railroad runs to a point above the highest fall, where small steamers ply to points well toward the sources of the Madre de Dios, Beni and Mamore, tributaries of the Madeira. Various points on all of these streams will be visited, according to the time available, and the party will then proceed by canoe or raft as far into the eastern Andes as possible, later crossing the mountains by mule-train and emerging via La Paz, at one of the Pacific ports. Should time suffice, a stop will be made on the return journey for an incursion into Colombia on the west side of the mountains, where some important drugs are to be found.

During about six months of the year that the exploration is expected to occupy, the party will be entirely isolated from civilized sources of support, and dependent on their own resources. Since the country abounds in fish and game, and since many sources of food-supply in the form of wild vegetation are known to Dr. Rusby, it would be possible to subsist largely on the natural food supplies of the country. The obtaining of such supplies, however, would consume much precious time that would otherwise be devoted to scientific collection and recording. For this reason, a food supply sufficient for the entire time will be carried into the wilderness. These supplies have been carefully selected, so as to provide a daily ration that is both wholesome and agreeable, since Dr. Rusby has learned by experience that many, if not most, of the ills from which such travelers suffer have their basis in poor nutrition. An ample supply of medicines will also be taken. Since one does not know what particular medicine may be needed, a full supply must be made available. Quinine, in the form of the bimuriate, will of course, be the principal item in this line. The onset of malarial fever may

be said to be impossible when the blood contains a sufficient amount of this alkaloid.

A full outfit of tents, cots, hammocks, bedding, canopies and camp equipment has been carefully selected. A large part of the stores have been purchased from the surplus stock of the U. S. Army.

It was originally designed to carry several of the folding canvas boats manufactured in Kalamazoo, but inquiry has developed the advice that these boats could not stand the rough waters to be navigated. The native river boats are very heavy, with thick and hard walls and can well resist the severe shocks resulting from striking upon the rocks in the rapids. At many points, of course, the boats must be taken out and portages made.

The party will of necessity be well armed, primarily in order to be able to secure such game as comes within reach, but also to guard against possible native hostility. Every precaution will be taken to avoid such encounters, and one of the surest ways of accomplishing this object is that of presenting a strong defensive position.

Among the drugs which it is expected will be encountered are tolu, ipecac of both species, simaruba, guaiac, copaiba of several species, manaca, guarana, muira-puama, caroba, several resins, coto and para-coto and cocillana.

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## LAW-MAKING, RATIONAL AND IRRATIONAL.\*

BY JAMES H. BEAL,

URBANA, ILL.

The faith of the average American citizen in the all sufficiency of legislation to cure social, economic and moral evils is child-like and bland—a faith that is never chilled by the fact that rarely in his experience has he known a law to accomplish more than a fraction of the good that was predicted of it, and that many laws have either failed altogether or have introduced greater or more numerous evils than those they were intended to cure.

The framers of the American system of government proceeded upon the theory that the people who were least governed—who had the fewest laws to obey—were the best governed. To-day this ancient and once honorable doctrine is very much in the discard.

\* Address delivered to Urbana Association of Commerce. Reprinted from the *Urbana Daily Courier*.

No matter what evil is under consideration, the first remedy thought of or proposed is legislation. The new bills introduced during the life of a single congress may run into the tens of thousands, and even a state general assembly may be called upon to consider more than a thousand proposed new laws during a single session.

Granting that our highly organized civilization, with predominating industrial and commercial interests, may require a more complex system of jurisprudence than would serve the necessities of a less specialized social organization, it is entirely absurd to assume that society needs the amount of regulation that these frantic attempts at law making would indicate. Comparatively few of the proposed new laws possess any real merit. A large proportion simply reflect the spirit of meddlesomeness that governs the minds of those who gratuitously assume both their right and their ability to prescribe the standards according to which their fellow citizens shall order their morals, their occupations and their daily lives.

Assuming that we shall continue to grind out national and state legislation at the present rate, what will be the volume of written law in another twenty-five years?

Consider also the bulk of secondary legislation in the form of rules and regulations adopted by the administrative officers of the law. Congress adopts a measure covering four or five pages, whereupon the department of administration issues a code of regulations covering fifty or sixty pages, introducing obligations and producing results which the original law making body could not have contemplated.

This country began its existence with the freest government on the face of the earth, and under the freest of governments our people have prospered as no people ever prospered before. Unless the present craze for law making can be checked, the next generation will find itself subject to more regulation than was old verboten-ridden Germany, and under the rule of more bureaus and bureaucrats than Russia under the czars.

#### THE INABILITY OF REFORMERS TO LEARN FROM EXPERIENCE.

Somehow men do not seem to learn, or at least do not heed, the lessons of experience in politics as they do the lessons of physical science.

In the physical sciences facts ascertained by careful experimentation are recorded in literature and become a part of the general in-

heritance of the race, so that men do not waste their lives in forever trying out the things that have been fully tested previously.

In political science, however, we do not seem to be able to record well established political and economic facts in such a way as to impress them upon the popular mind and save the world from endlessly trying over and over the same old experiments that have been tried and have failed numberless times before. These facts have been recorded, however, and are available to those who will take trouble to look for them.

SUCCESSFUL LAWS MARK REFORMS BUT DO NOT MAKE THEM.

One of the facts we may learn from the history or political experiments is that successful laws do not make reforms, but only mark them, that is, they mark the periods when the reforms have so far gained the consent of the minds and hearts of the people that the written statutes are merely concrete expressions of the will of a liberal majority of those who are to live under them.

If a proposed reform will really make the world a better place to live in, it is necessary only to convince a majority of the people of its wisdom and desirability when appropriate legislation will follow logically and naturally. Generally, however, the radical reformer resents the slow and cumbrous methods of education and prefers to make an organized assault upon the law making body and compel an immediate acceptance of his alleged reform by act of legislature.

When the premature law is openly derided and violated with comparative impunity, the reformer will not admit, and probably does not realize that the legislation was in advance of genuine public sentiment. His remedy is to adopt still more legislation of the same kind, piling prohibition upon prohibition and penalty upon penalty, with the result of producing an ever increasing number of violations, and a diminished respect for the law.

If mere law making could make men or society perfect, the world would have been free of evil millenniums ago. Every known political and social tort has been legislated against thousands of times and yet these wrongs persist, and not a few when traced to their sources will be found to be the direct outgrowth of the very laws intended to prevent them.

REFORM LEGISLATION IMPOSES BURDENS UPON INNOCENT PEOPLE.

Another fact to be learned from the history of experiments in law

making is that reform measures invariably impose burdens upon perfectly innocent people who do not stand in need of reformation and invariably place restrictions upon acts that may be wholly without evil or even meritorious.

This has been true of every piece of reform legislation that has ever been placed upon the statute books. The best of reform measures are mixtures of good and evil, and not a few alleged reform measures have been responsible for the growth of greater evils than those they were intended to cure.

Common sense therefore demands that we take into consideration the burdens a proposed law will certainly impose upon innocent people and upon innocent industries as well as the good results which it is hoped the law will produce. Like other things, a reform law may some times cost more than it is worth.

The exact point at which the evils of a reformatory law begin to outweigh the good cannot be determined with certainty in advance of actual trial, but experience teaches that it usually falls short of the extreme limit which the radical reformer is inclined to demand.

#### EXCESSIVE REGULATION PRECEDES THE DESTRUCTION OF LIBERTY.

Another fact constantly brought to the attention of the student of political history is that peoples who have obtained their liberties by the most heroic of sacrifices have so frequently thrown them away again in the frivolous pursuit of things they thought would make their liberties still more secure and their freedom still more free.

The story of the democracies that have failed shows that their vigor and prosperity regularly declined with the growth of internal legislation, or with the forcing of obnoxious regulations upon their citizens by the factions which successively obtained control, until they had so weakened themselves by internal strife that they fell to pieces of their own weight or were an easy prey to enemies from without.

Of course, no people ever intentionally destroyed their own liberties. They always intended their law making to make their countries better and stronger. Their uniform mistake was in consenting to the violation of fundamental principles for the sake of some fancied immediate good which their radical legislation was expected to accomplish.

The one great lesson of all these unsuccessful attempts at self-

government is that a nation which willingly submits to the suspension of the principles of free government for the sake of expediency, or for the accomplishment of some quick and immediate reform will in the end always come to grief. Principles that can be suspended for beneficent purposes can also be suspended for evil purposes, and laws intended for purely good ends can also be enforced oppressively.

THE FUNDAMENTAL PRINCIPLES OF FREE GOVERNMENT ARE  
PERMANENT.

Another lesson from the history of political experiments is that the fundamental principles of free government do not vary with the changing values of the factors of civilization. A principle of government essential to the preservation of liberty in one age is essential to the preservation of liberty in every age.

By certain doctrinaire reformers of the present day the United States constitution is considered to be obsolete and out of date because it was composed before the age of telephones, wireless telegraphy and flying machines. It would be as reasonable to consider the principles of arithmetic as obsolete because they were discovered before the invention of modern business methods.

Civil government is not a problem of mechanics but of human nature, and no group of men who ever lived had a keener or closer information of the essential qualities of human nature than the statesmen who formulated the federal constitution and the bill of rights that was made a part of that document. They were not only men of rare natural ability but they met their task, with a face to face directness and with a freshness of experience with governmental tyranny that their successors have not had.

These men said: No government has ever had unlimited power over the lives and destinies of its people that it did not eventually exercise its powers oppressively. We will prevent such a disaster by making it a fundamental principle of the federal constitution that the powers of the government shall be limited strictly to matters of general concern, and will prohibit its interference in the lives and liberties of the individual citizen, except in so far as they are intimately and directly connected with the powers expressly given. Similar considerations induced the placing of corresponding limitations upon the powers of the governments created by the earlier state constitutions.



The doctrinaires are now ready to tear these old and well tried charters of liberty to pieces and to confer upon the legislative and executive departments the very powers which the elder group of statesmen were certain should be withheld from them. Perhaps the doctrinaires are right; but if our government can possess unlimited powers without using them oppressively, it will be the first instance of its kind in all the history of civilization.

NO LAW CAN BE 100 PER CENT. EFFICIENT.

Another lesson of political history is that even the best of laws will fall far short of complete efficiency in removing the evils at which it is aimed. Whether we have one law or a thousand upon a given subject, there will always be a residuum of evil that mere law making will not cure. When this irreducible minimum has been reached the multiplying of prohibitions only multiplies the number of violations.

It is an accepted principle in mechanics that no machine can be expected to reach 100 per cent. in practical efficiency, and the mechanician therefore directs his efforts to obtaining the most profitable ratio of power expended to work delivered. Strangely enough, people who do not expect to obtain one hundred per cent. efficiency from any construction of wood or metal, are forever trying to compose laws that shall be one hundred per cent. efficient, that is to say, laws that cannot be or that will not be violated.

Some thousands of years ago there was promulgated a code of ten commandments governing the fundamentals of social and moral conduct, and in all the centuries since then the divine author of that code has neither repealed nor amended a single one of the ten original articles. A divine intelligence could be expected to understand that if men are disposed to disobey the commandments of a primary code they will be equally disposed to disobey the provisions of all subsidiary codes of amendments and regulations, but human law makers, when they discover that one set of statutes is being violated, seem to imagine that by the adoption of a new code of regulations, or by rearranging the phraseology of the old code, the law violator will become a law observer.

The law making bodies of this year are busy amending and reforming the laws adopted at previous sessions. Last year they were doing the same thing. Next year they will be repeating the process.

Each successive measure in its day was proposed as an important and necessary reform, and those who dared to oppose it were denounced as reactionaries and obstructionists, or worse. When in time its defects became evident, it was then attacked as an abuse by a new set of law makers, the successive crops of reformers jumping over each other's heads like a group of boys at leap-frog.

What we all must learn is that the best possible law will fall considerably short of perfection, and that when any comprehensive and well considered law has once been placed upon the statute books our attention should be given to its enforcement, and not wasted in impossible attempts to devise measures that cannot be violated.

#### EXCESSIVE AND RADICAL LEGISLATION PRODUCTIVE OF LAWLESSNESS.

Another lesson of political history that many reformers have failed to learn is that excessive and extreme legislation is of itself a most potent breeder of lawlessness.

Every student of history knows that, without exception, periods of excessive and radical regulation have always been followed by periods of equally extreme and radical reaction.

Seemingly there is a certain ration or balance of regulation that must be maintained to obtain the best results for law and order. Human nature will stand for coercion without reaction up to a certain limit, but if this limit be exceeded there will be a moral break down that makes the individual less amenable to the reasonable restraints of the law than before.

The very extremity of a law may constitute the most potent reason for its violation. In other words, the profits of violating the law may be so great, and the risk of punishment so small in comparison that the hazard is really not much greater than the hazard of lawful occupations that are much less profitable. Such laws in effect place a premium upon law breaking, and penalize the law-abiding. Citizens who are naturally inclined to obey the law find themselves at a disadvantage as compared to those who ignore it, and there is a letting down of moral tone all along the line.

Most men believe that the chief function of government is to protect them from oppression. When the citizen comes to feel that the government itself has become an oppressor he is already at heart a potential law breaker, ready to evade the mandates of the law whenever he thinks it safe to do so.

### THE FAILURE OF EMOTIONAL LEGISLATION.

That some laws succeed fairly well in correcting the evils at which they are aimed all can testify from personal observation, that some laws do not work at all, or have a back action that is worse than inaction, is a matter of common knowledge.

If we examine into a law that is known to work fairly well in practice we shall usually find it to be one that is not extreme in its provisions, and one that was formulated by cool and deliberate judgment in the light of well established precedents. If we examine into the laws that are admitted failures we shall find almost universally that they are extremely drastic in their provisions, that they were composed under the influence of strong emotions and passed under the whip of intensive propaganda.

When our emotions are aroused in public affairs we want direct action and lots of it, and we mistrust the motives of those who urge less drastic measures as a more certain, though slower and less spectacular method of reaching the desired end.

We regulated the railroads with our emotions instead of with reason and judgment until we regulated them nearly into bankruptcy. Now at tremendous cost we are painfully trying to work back to the line of reason and moderation.

When we undertook to regulate the trusts we again rejected the teachings of experience and the reasonable judgment of experts and followed emotional leadership with the result that we hobbled and altered legitimate business enterprises without materially curbing the operations of those the law was intended to reach. This emotionally formulated law has not only operated to prevent small business men from combining to protect themselves from the aggressions of large capital interests, but every time Congress has passed an appropriation bill it has been reduced to the pitiful expedient of expressly providing that the money appropriated shall not be used to prosecute violations of the law by certain strongly organized interests.

Why is it that we have so frequently followed emotional leaders and rejected the counsel of conservative statesmanship? Simply because of our impatience for immediate results. It is the same disposition that prompts the teacher or doctor or merchant to withdraw his small hoard from the security of the savings bank and invest it in oil stock that promises a thousand per cent. return.

Common horse sense, or even average mule intelligence should teach us that in political affairs as in business enterprises the more profuse the promises the less likely the performance. The promotor of "get-rich-quick" concerns can always promise greater returns on the investment than can be offered by the promoters of legitimate business undertakings.

LAWS FAIL, WHEN THEY IGNORE HUMAN NATURE.

Another lesson from the history of political experiments is that laws also fail when they ignore the ordinary qualities of human nature instead of operating in harmony therewith.

The engineer who digs a tunnel, or drains a swamp, or irrigates a desert, does not begin operations without a careful and scientific study of all the surrounding conditions. Sometimes he finds a direct method of approach the most suitable, sometimes an indirect approach, and his success is measured by his ability to adjust his methods to the peculiar circumstances in each case. Sentiment and emotion find no place in his plans. He does not attempt to destroy the natural tendency of water to flow down hill, but makes use of a fall of water at one place to carry water up hill at some other place. He does not ignore or attempt to violently suspend the operation of natural laws, but seeks to utilize them in the attainment of his purpose.

The reformer of political and social institutions, in his anxiety for direct and immediate results, rarely takes time to patiently study the particular conditions involved, refuses to be bound by the laws of human nature, and will not consider any other method of approach than the age-old formula, "it is forbidden," which in the history of civilization has failed as often, if not oftener, than it has succeeded.

Some evils of the body politic are of such a nature that the only proper course of procedure is to totally prohibit them, but others are like the tares in the wheat that cannot be directly uprooted without uprooting the wheat also.

Human nature in the mass can be led by education and persuasion, it cannot be successfully driven. Laws that are passed by tricky political methods or adopted with the grudging assent of a bare majority, and which attempt to violently uproot world-old prejudices or beliefs in a day retard rather than advance genuine reform.

WE TALK EUGENICS AND PRACTICE ANTI-EUGENICS.

One who should study the accomplished and attempted legislation of the last quarter of a century might reasonably arrive at the conclusion that the chief object of civil government is to protect the mentally incompetent, the morally weak or vicious and the physically unfit. He would observe, for example, that the law makes it difficult to secure useful and necessary drugs for the treatment of the mentally and morally competent in order to keep them out of the hands of degenerates who might use them to their own hurt. He would discover legislation to handicap the enterprising and progressive business man in order to enable the less enterprising and less progressive to succeed. He would note the legislation of trade union rules designed to penalize the skilled and industrious artisan and prohibit him from producing more or better work than the unskilled and lazy. He would discover numberless schemes, either accomplished or in process of accomplishment, designed to pension the lazy, incompetent and wasteful members of society and to collect the pensions from the industrious, competent and economical members. He would observe parlor philosophers talking about the importance of developing a mentally fit and physically strong and virile race and advocating governmental and social policies designed to produce the opposite.

Since we have such an abundance of societies and devices intended to favor and protect weaklings and degenerates, would it not be timely for humane people to establish a society to protect the rights of those who are neither weak nor vicious, who exercise a proper restraint upon their appetites and passions, who are industrious and thrifty, and in every way prove their right to respectful consideration?

Is it not time to return to the viewpoint of the fathers of the republic as to the proper functions of government, and to realize that the sane and decent members of society possess certain inalienable rights of which they should not be deprived in order to confer special benefits upon those who do not deserve, or who have abused the privileges of citizenship?

No good citizen would willingly oppose any sane attempt to reform whatever may be amiss in our social or political institutions, but surely we are entitled to demand that such reforms be framed with due regard for the rights of the innocent bystander.

## STANDARDIZATION OF TINCTURE OF STROPHANTHUS.\*

BY C. T. BENNETT, B.Sc., F.I.C., F.C.S., PHARMACEUTICAL CHEMIST.

Without attempting to carry out the elaborate researches suggested in the Conference Research List, I venture to put forward a few suggestions for the consideration of a future Pharmacopoeia Revision Committee.

The variation in strength of tincture of strophanthus was the subject of a note by my late chief, Mr. J. C. Umney, published in *The British and Colonial Pharmacist* of December, 1918, p. 375. In this note it was pointed out that the standards adopted for physiologically testing this potent drug differed considerably, the minimum lethal dose calculated for a 100 Gm. frog being as follows for various commercial samples:

M.L.D. for 100 Gm. Frog.

U. S. P. standard (1 hour).....	0.006 Cc.
Standard adopted by the Society of	
Apothecaries.....	0.020 (since altered to 0.01 Cc.)
Sample "A" (time not stated).....	0.007 Cc.
Sample "B" (time not stated).....	0.020 Cc.
Sample "C" (time not stated).....	0.050 Cc.
Sample "D" (2 hours).....	0.150 Cc.
Sample "E" (2 hours).....	0.150 Cc.

If the standards adopted vary to such an enormous extent as shown by these figures, then it is obvious that physiological standardization will fall into disfavor unless an international standard be agreed upon.

According to Rowe (*Y. B. P.*, 1917, p. 264), commercial samples of strophanthus tested physiologically have shown enormous variation in potency, but since 1913 samples examined by him have been much more uniform. He takes exception, however, to the use of ouabain or gratus-strophanthin as a standard, and considers that crystalline Kombé strophanthin is the proper standard.

The strength of the tincture official in the British Pharmacopoeia, 1914, is four times that of the 1898 tincture, *viz.*, 1 in 10 by volume (100 Gms. of the seeds in 1000 Cc. of tincture) in accordance with the International Agreement of 1906, and identical in strength with that of the United States Pharmacopoeia, except that the latter is prepared with 95 per cent. alcohol.

\* Reprinted from *The Pharmaceutical Journal and Pharmacist*, July 24, 1920.

The questions to be considered are as follows:

1. Is *strophanthus* of sufficient importance to the medical profession to warrant a thorough investigation of the glucosides found in the various species?

In reply to this I can only repeat Mr. Umney's statement that tincture of *strophanthus* is rapidly going out of use owing to its variable strength and the uncertainty of its results.

2. As at the time of writing it is impossible to obtain unmixed seeds of *Strophanthus Kombé* (which are alone official in the British Pharmacopoeia) in sufficient quantity to meet the demand, which variety would be the best substitute? This question can only be answered by a more thorough investigation of the various species.

3. Is it practicable for the collection of the most suitable variety to be under the supervision of a competent botanist? It should be possible for the importers to make some arrangements for this, even if higher prices had to be paid for the seeds.

4. Could the glucoside *strophanthin*, which is official in the United States Pharmacopoeia and in the French Codex, or a preparation of it, be employed to replace the tincture in pharmacy? If the glucoside, or mixture of glucosides obtained from a definite species were made official, then it would be desirable to describe its characters in order to ensure the purity of the product and uniformity of medicinal action. Unfortunately, the chemical and physical characters of the various glucosides found in the different species are not sufficiently known for the fixing of a definite standard.

I do not propose to burden this note by summarizing the researches carried out by various workers on the glucosides found in the different species, especially as the results are considerably at variance, but I would like to point out that no definite standard is laid down by the U. S. P. monograph for *strophanthin*, while the French Codex gives a melting point of  $185^{\circ}$  for *strophanthin* obtained from *Strophanthus hispidus*. According to Cohen (*Y. B. P.*, 1913, p. 134) *h*-*Strophanthin* from *S. hispidus* sinters at  $160^{\circ}$ , but does not melt at  $190^{\circ}$ , *g*-*Strophanthin* from *S. gratus* sinters at  $185^{\circ}$ , and *k*-*Strophanthin* from *S. Kombé* sinters at  $170^{\circ}$ .

5. If physiological standardization is to be adopted, what is the best method of procedure?

Possibly an agreement could be arrived at between the respective Revision Committees of the British and United States Pharmacopoeias. The chief objection to physiological standardization is that

the action on a frog may be very different from that on a human being. In physiological tests no attention is paid to the age of the frog.

6. If physiological tests are not thought desirable, is a chemical method necessary and practicable? Although the chemical methods which have been proposed have some disadvantages, it seems desirable that a standard for the seeds should be fixed by the British Pharmacopoeia, as this procedure would at least ensure an approximately uniform tincture.

The standardization of strophanthus must, therefore, be undertaken either by the botanist, the physiologist, or the chemist, or preferably by the coöperation of all three, if we are to ensure uniformity of strength. As a chemist, I am strongly in favor of chemical assay, and a review of the processes has led to the conclusion that Barclay's method as modified by Haycock is the most suitable for general adoption. (See *Y. B. P.*, 1911, p. 125.) The standard I would suggest for the seeds is 6 per cent. to 8 per cent. of strophanthin or 0.6 per cent. for the tincture.

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### COLOR TEST FOR OXALIC ACID.\*

BY LEWIS H. CHEINOFF

DENVER, COLO.

A few crystals of resorcinol are added to about 5 Cc. of the unknown solution in a test-tube, and the mixture is warmed slightly to dissolve the resorcinol. It is then cooled and 5 Cc. of conc. sulphuric acid is carefully and slowly poured in along the side of the tube so as to form a layer. A blue ring will be formed at the junction of the 2 layers, if oxalic acid is present. The color is best seen if held to the light in front of a sheet of white paper. Care must be taken that the mixture does not warm up appreciably. If the blue color does not appear in a few minutes, the mixture is shaken thoroughly, and, after cooling somewhat, 5 Cc. more of sulphuric acid is added. Should the color still fail to appear, the mixed contents of the tube should be gently warmed over a flame (not boiled) when an indigo blue color will diffuse throughout the liquid. If the mixture be cooled with ice-water, the color will disappear only to

\**Journal Amer. Chem. Soc.*, Sept.



reappear again on heating. If the mixture be boiled a few minutes, the color will turn a deep dark *green*, which will become a light yellow-green on cooling. If to the cold yellow-green solution an equal volume of sulphuric acid be added so as to form 2 layers, the *blue* color will again appear. It is believed that all these reactions taken together are characteristic of oxalic acid alone.

This test may be made sensitive to one milligram if the dry unknown substance be warmed with 2 drops of a 10 per cent. aqueous resorcinol solution and the sulphuric acid added drop by drop. The blue color then appears immediately. For very dilute solutions of oxalic acid or its salts, it is best to evaporate to a concentration of about 10 per cent.

If interfering substances are present the oxalic acid may be precipitated in ammoniacal solution as the calcium salt, washed with water, and the test applied directly to an aqueous suspension of the salt.

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## CURRENT LITERATURE.

### TRADE INTEREST.

ALSATIAN POTASH.—The French Minister of Agriculture, in a notice published in the *Journée Industrielle*, reminds persons interested in the purchase of Alsatian potash salts, that trade in this commodity is now free. He adds that orders for potash are no concern of his Department, and that they should be sent either to Mulhouse, or to the various representatives of the Société Commerciale des Potasses d'Alsace. Whereas before the war the consumption of pure potash in France did not exceed 37,000 tons a year, the mines of Alsace were able to send to France no less than 47,000 tons of pure potash in the year 1919, and 30,000 tons in the first half of the present year. Many orders which were given sometime ago have not yet been delivered, but the Minister of Agriculture has been able to arrange that a sufficient number of trains shall be placed at the disposal of the mines, to insure the delivery of 5,000 to 8,000 tons of pure potash a month. It is, therefore, to be presumed that delays in delivery will no longer occur. (From *The Pharm. Jour. & Pharm.*, Sept. 4, 1920.)

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## MEDICAL AND PHARMACEUTICAL NOTES.

THE CLINICAL SIGNIFICANCE OF CYLINDROIDS.—On the basis of examination of 81 cases of uncompensated heart disease, Eigenberger reports that his results confirm the views of von Jaksch and Quensel, who ascribe to cylindroids a certain clinical importance as signs of disturbance of renal circulation. Eigenberger could demonstrate cylindroids in 36, or 44 per cent., of his 81 cases. In most of the cases in which cylindroids were present there were strong clinical signs of disturbed renal circulation. In 2 of the cases with large number of cylindroids, necropsy disclosed marked renal stasis. (From *Zentralblatt für innere Medizin, Leipzig*, May 15, 1920, 41, No. 20; through *Jour. Amer. Med. Assoc.*, August 28, 1920.)

BETTER WAY TO GIVE BENZYL BENZOATE.—To overcome the unpleasant, bitter, burning taste of the alcoholic solution of benzyl benzoate Hirschfelder gives pure benzyl benzoate, 10 parts; emulsion of acacia, 5 parts; elixir eriodictyon aromaticum (N. F.), 35 parts; dose, one teaspoonful. He has been able to secure relief of symptoms in a considerable number of cases of conditions caused by spasm of smooth muscle, cardio-spasm, pylorospasm; pain in gastric ulcer from aspartic constipation. The relief occurs within half an hour after taking and lasts. Benzyl benzoate brings about relief in many, but by no means all, cases of bronchial asthma, just as is true of atropine or other drugs that inhibit the vagus. Still more striking results have been obtained in the treatment of dysmenorrhea. About 80 per cent. of the patients have had relief from pain after from one to three doses. (From *Minnesota Medicine, St. Paul*, August, 1920, 3, No. 8; through *Jour. Amer. Med. Assoc.*, August 28, 1920.)

VALUE OF COLLOIDAL GOLD TEST.—The results of other workers regarding the value of the colloidal gold test in the diagnosis of general paralysis are confirmed by Cruickshank. The substance in the spinal fluid of general paralytics which causes precipitation of colloidal gold is not dialyzable and resides in the globulin fraction of the protein and in this respect resembles the Wassermann reacting substance. It is not altered by heating to the coagulation point of protein. The reaction is not due to peptone. The various types of reaction can be simulated by mixtures of globulin and albumin, the globulin acting as a precipitating agent and the albumin

as an inhibitory or protective one. Syphilitic reactions are due to an amount of albumin sufficient to obscure partially the precipitating effect of the globulin. As the globulins obtained from negative spinal fluids, even when used in concentrated form, are almost inactive, the precipitating action of paretic fluids cannot be ascribed solely to the increase in globulin, but is probably dependent on a specific alteration of the physical state of the globulin, which is associated with a positive electric charge. Human serum globulin has the characters of a positive colloid, but the paretic and syphilitic reactions of spinal fluids cannot be attributed merely to the passage of serum globulin into the spinal fluid. The meningitic reactions, on the other hand, may be due to the leakage of plasma through damaged meninges. (From *British Jour. of Exper. Pathology*, London, April, 1920, 1, No. 2; through *Jour. Amer. Med. Assoc.*, August 28, 1920.)

BENZYL BENZOATE IN WHOOPING COUGH.—The number of cases studied by Macht was about 115. All these cases were characterized by whooping and in many the paroxysms were accompanied by vomiting and small hemorrhages. Most of the patients before coming under Macht's observation had been treated by parents or doctors with paregoric and other popular drugs without any benefit, while others had been left alone without any treatment whatever. A number of the patients received vaccine treatment, but the results in these cases were also not at all striking. All other medication was discontinued and the patients were given a 20 per cent. solution of benzyl benzoate by mouth. The dosage varied from 5 to 40 drops in water three or four times a day and oftener, depending on the age of the patient and the severity of the disease. In cases in which the simple alcoholic solution of benzoate was found to be too distasteful to the young patients it was flavored with a few drops of benzaldehyde and the medicine was administered in sugar, water or milk. The addition of a little benzaldehyde to a solution of benzyl benzoate in amounts varying from 1 to 5 per cent. produced a mixture which seemed to act more effectively in cases of whooping cough than benzyl benzoate alone. It was found that the administration of benzyl benzoate in the form of a suspension in simple elixir, in syrup of yerba santa and other syrups or elixirs was not a satisfactory method either of disguising the taste or administering the drug over long periods of time. About

90 per cent. of all the patients showed more or less beneficial effects; about 50 per cent. exhibited marked improvements in the symptoms. The therapeutic effects of benzyl benzoate were not of a curative character but were of a distinctly palliative nature. (From *Bull. of Johns Hopkins Hospital*, Baltimore, 12: No. 4 (July), 1920; through *Jour. Amer. Med. Assoc.*, August 28, 1920.)

**BENZYL BENZOATE FOR PERSISTENT HICCOUGH.**—The value of the new antispasmodic benzyl benzoate has lately been demonstrated in the treatment of persistent hiccough. Three cases are recorded which were eased by the drug in a very short time, all of which had resisted ordinary treatment. One case was cured by the administration of one dose of 25 drops of a 20 per cent. solution in alcohol, equivalent to 5 minims of benzyl benzoate. It is suggested that the drug should prove of diagnostic value in differentiating hiccough of purely central origin from that of peripheral origin. As the chief effect is on smooth muscle, it should prove useful for the relief of the latter. Benzyl benzoate is best administered in the form originally suggested by the author, namely a 20 per cent. solution in alcohol. Of this solution the patient takes 20 to 40 minims in water or milk. It is neither convenient nor advantageous to give the drug in suspension in syrups or elixirs; and the administration in capsules has produced irritation in some cases and rendered the therapeutic action too slow in others. To children the solution can be conveniently given in sugar, water or milk. (*Med. Record; Lancet*, 199, 512, 1920; through *Pharm. Jour & Pharmacist*, September 11, 1920.)

**INFUSION OF PARSLEY FOR GALL STONES.**—Attention is drawn by H. C. Kidd (*B. M. J.*, Aug. 14, 1920, p. 244) to the use of infusion of parsley in the treatment of gall stones. A lady over 70 years of age had suffered for many years from this trouble, with severe colic and jaundice. In November, 1918, she had a prolonged attack, which reduced her to the lowest extremity. In the region of the gall bladder was a large palpable mass in which gall stones could be felt. She was advised to undergo an operation but refused; and, having heard of a friend who had been cured by drinking infusion of parsley, she gave this remedy a trial. A double handful of fresh parsley leaves was soaked in cold water, which was afterwards brought to the boil, strained, and allowed to cool. She took a pint and a half daily of this infusion and in time this seemed

to cure her. She is now free from pain and sickness; the mass felt in the gall bladder has disappeared, and her general condition is satisfactory.

Dr. Kidd seems to have been unable to trace any reference in the literature to the use of parsley for this purpose, but we would point out that "compound mixture of agrimony," of which parsley is an important ingredient, has been in use in the north for many years as a remedy for gall stones. This mixture is an infusion containing parsley, barberry, agrimony, toad-flax (*antirrhinum*), taraxacum, caraway, chamomile, and rhubarb, the doses being half an ounce thrice daily. (From *The Prescriber*, October, 1920.)

EMETINE BISMUTH IODIDE: A NEW VEHICLE.—The difficulty of administration of emetine bismuth iodide has always been the fact that a portion of the drug is dissolved in the stomach, with resulting nausea. T. J. G. Mayer (*J. Trop. Med.*, May 1, 1920) claims to have found a vehicle that will carry the drug safely through the stomach. The drug is rubbed up with 16 parts of mutton fat, the mass moulded into rounded pills weighing about 7 grains, and each pill covered with a layer of mutton fat, applied with a paint brush. The mutton fat being solid at body temperature is not digested until it is too far beyond the pyloric orifice to be regurgitated and cause vomiting or even nausea. Pills containing one and one-half grains of the drug and about seven and one-half grains of mutton fat are about as large as may be conveniently swallowed. (From *The Prescriber*, October, 1920.)

MONARSONE: A NEW ANTISYPHILITIC.—A new arsenical compound for the treatment of syphilis is described by B. L. Wright *et al* (*Med. Record*, April 10, 1920). The substance in question is disodium monoethylarsone,  $\text{CH}_3\text{CH}_2\text{AsO}(\text{NaO})_2$ , which for brevity they call *monarson*. It contains 7 per cent. more arsenic than arsenobenzol; is decidedly less toxic than the arsenobenzol compounds; is perfectly soluble in small quantities of water, and may be given without danger in solutions containing 0.2 Gm. per Cc. Monarson has no haemolytic action on the red corpuscles, and may be given intravenously without fear of extravasation, as leakage causes no untoward effect. It requires no special apparatus for its administration, and its solutions are so stable that they resist oxidation or decomposition when boiled or subjected to the higher temperatures of the autoclave. (From *The Prescriber*, October, 1920.)

RAPID PREPARATION OF MERCURIAL OINTMENT.—The addition of lanoline to the lard in which mercury is to be divided in making mercury ointment is one of the most efficacious methods of overcoming the difficulties encountered in incorporating the mercury. Considering that the action of the lanoline is due to its content of cholesterin, Dr. G. Fontes has experimented with the addition of that substance to lard with and without the subsequent admixture of water and reports the following results:

100 Gms. lard, with 2.5% cholesterin immediately absorbed 490 Gms. mercury.

100 Gms. lard, with 2.5% cholesterin and 20 Gms. of water absorbed 575 Gms. mercury.

100 Gms. lard, with 2.5% cholesterin and 50 Gms. of water absorbed 970 Gms. mercury.

100 Gms. lard, with 5% cholesterin absorbed immediately, 1,500 Gms. mercury.

100 Gms. lard, with 5% cholesterin and 100 Gms. of water absorbed 1,900 Gms. mercury.

100 Gms. lard, with 5% cholesterin and 160 Gms. of water absorbed 3,000 Gms. mercury.

The lard and cholesterin were melted together, the water was then incorporated and to the mixture the mercury was added in small portions stirring with a pestle. The metal was rapidly incorporated (extinction parfait). Ten minutes trituration sufficed to make the ointment. The product may be readily diluted with a fatty material or with petrolatum. (*J. Pharm. Chim.*, 1920, p. 195.)

J. F. C.

BENZYL BENZOATE IN HICCUP.—Macht has found benzyl benzoate to be an invaluable medicine in the treatment of persistent hiccup of both adults and children. Not only has it been found useful in allaying the ordinary mild forms of hiccup so common in infants, but the drug has been found to be efficient in stopping those forms of hiccup termed pernicious, that is, those cases in which the phenomenon persisted for long periods of time, from twenty-four hours to several days, and in which the singultus was unaffected by all other forms of medicinal treatment, both external and internal. Macht believes that benzyl benzoate also is of diagnostic value in differentiating between the hiccups of a purely central origin, on the one hand, and those which are due to some peripheral origin, on the other. In as much as benzyl benzoate exerts its chief effect peripherally on the smooth muscle structures, the author is inclined to

believe that this drug may be most useful in the treatment of hiccups of peripheral origin. The benzyl benzoate exerts its action best when given in a 20 per cent. solution in alcohol. Of this solution the patient is directed to take from 20 to 40 drops in water or milk. The author has not found it either convenient or advantageous to administer the drug in suspension in various elixirs or syrups, and administration in capsules has been found by him in some cases to produce local irritation, and in others to render the therapeutic action too slow. To children the solution can be conveniently administered in sugar, water or milk. (From *Medical Record*, New York, Jul. 24, 1920, 98, No. 4; through *Jour. Amer. Med. Assoc.*, Aug. 21, 1920.)

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#### NEWS ITEMS AND PERSONAL NOTES.

OFFICERS ELECT OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.—The tellers report, that as a result of the mail vote, the following officers of the American Pharmaceutical Association have been elected for year 1921-1922:

President, Samuel L. Hilton, Washington, D. C.

First Vice-President, Charles E. Caspari, St. Louis, Mo.

Second Vice-President, David F. Jones, Watertown, S. D.

Third Vice-President, Hugo H. Schaefer, New York, N. Y.

Members of the Council for three years, Henry M. Whelpley, St. Louis, Mo.; George M. Beringer, Camden, N. J.; John G. Godding, Boston, Mass.

Also that the proposition submitted to a referendum vote, to raise the annual dues from \$5.00 to \$7.50 and to continue the publication of both the *Journal of the American Pharmaceutical Association* and the *Year Book* was carried by a substantial majority.

THE AMERICAN DRUG MANUFACTURERS' ASSOCIATION, ANNUAL MEETING AND NEW PRESIDENT.—The next annual meeting of the American Drug Manufacturers' Association will be held in New York City, April 11-14, 1921. The headquarters hotel will be announced later.

Mr. W. A. Sailer, of Sharp & Dohme, has been elected as President for the unexpired term of the late President R. C. Stofer.

NEWLY ELECTED HEAD OF THE NORWICH PHARMACAL COMPANY.

Mr. W. G. Peckham, Second Vice-President and General Sales Director of the Norwich Pharmacal Company has been elected President of that corporation, filling the vacancy caused by the decease of R. C. Stofer.

Mr. Peckham received his early pharmaceutical training in the organization of which he is now the head, having been engaged when sixteen years of age as errand boy in the tablet department.



W. G. PECKHAM.

After six years' experience in which he became an expert tablet man, he accepted a position as foreman of the tablet department of the Geo. L. Clafin Company—wholesale druggists of Providence, R. I., who conducted a manufacturing laboratory in connection with their wholesale business. A year later, at the formation of the Daggett and Miller Company, he became Superintendent of their laboratory and later on, Vice-President and General Manager.

About ten years ago he returned to his first employers as Assistant.



Manager of their Chicago branch. A year later, he was made manager which position he has since occupied up to his election as President. In this position he demonstrated exceptional ability and under his régime the business has trebled.

Mr. Peckham is a young man—under forty-five—but his broad knowledge, energy and years of experience in handling the affairs of the Company's largest branch have well fitted him for the presidency of this prominent pharmaceutical industry.

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### BOOK REVIEWS.

MARGARINE. By William Clayton, M.Sc. Longmans, Green & Co., London. 187 pages, cloth bound. Price, \$4.75.

The series of monographs on Industrial Chemistry, edited by Sir Edward Thorpe, has been added to by the publication of this excellent work on Margarine, the first of its kind in any language according to the author.

The work includes a consideration of Oils and Fats Used in Margarine Manufacture, Edible Hydrogenated Oils, Milk Examination, Margarine Manufacture, Theory of Emulsification, Butter and Renovated Butter, Analysis of Butter and Margarine, Deterioration of Butter and Margarine in Storage, Nutritional Chemistry of Fats and Oils.

The book is illustrated with many half-tone plates and figures in the text and contains a complete bibliography of the subject occupying thirty-five pages in the appendix. There are three separate indexes, one for authors, one for patents (American, English and German), and a very complete subject index.

The book as a whole is of particular interest only to the food chemist or food law enforcement officer, but the chapter on the theory of emulsification, which is very complete and up-to-date, makes the book a worth while addition to any scientific library.

C. H. LAW.

THE DETERMINATION OF HYDROGEN IONS. By W. Mansfield Clark, M.A., Ph.D., Chemist, Research Laboratories of the Dairy Division, United States Department of Agriculture. 8vo., 309 pages and index. Williams and Wilkins, Baltimore. \$5.00.

The theory of ionization was set forth by Arrhenius in the first volume of the *Zeitschrift fuer physikalische Chemie*, in 1887. As

with all other notable theories or principles in science, foreshadowings of some features of it can be found in the works of earlier scientists, but it is not the one who first "thinks of" anything, but the one who "thinks it out" or establishes it that deserves the greater honor. Dr. Clark informs us in his preface that Pasteur had a distinct perception of the importance of the degree of acidity, although, of course, he did not formulate this in the terms of dissociation or ion concentration. Pasteur pointed out, in his *Studies on Fermentation*, that the relatively high acidity of must favors a natural alcoholic fermentation, while the low relative acidity of wort introduces difficulties in the brewing of malt liquors. There is here probably a theme for an interesting and useful disquisition on the influence of hydrogen ion concentration on the progress of civilization. One writer has declared that the limits of the Roman Empire in northwestern Europe were, in a measure at least, determined by the food and beverage habits of the races. The Romans and their principal auxiliaries were accustomed to wine and olive oil; the tribes of Baltic region used beer and butter. We have good reason to believe that butter is more nutritious than the vegetable oils. The materialistic conception of history has been a prominent theme in later days; is it possible that the world's progress and the solution of the problem of the league of nations will be reduced finally to an equation involving  $\log. p_H$ ?

We are dealing, however, with a work of special type and of novel purpose. Chemists have, at last, the important and difficult problems of hydrogen ion concentration presented in extended and careful manner and explained in detail. Dr. Clark points out that of all the secondary inferences drawn from the general theory of ionization, the most important is that relating to the resolution of "acidity" into two components—the concentration of hydrogen ions and the quantity of acid capable of furnishing those ions. For two reasons the concentration of the hydrogen ion occupies a unique place in the phenomena of ionization. The factor of concentration is now known to be of very great importance in biologic chemistry. Already, many data have been collected as to the extent which the soil acids are ionized, and in this connection, it must be noted that the older methods which merely determined the total acidity by titration, for instance, with alkali, do not give the real reaction of the soil solution to the living tissues with which they are in contact. It is a question, indeed, whether, in the light of the development of

this phase of the subject, a large part of the earlier data of soil analysis may not have to be scrapped. Another point about hydrogen ion concentration is that at present the determination of it is among the most satisfactory of ordinary laboratory processes. Of course, as Clark points out, there is danger of making the subject a fetish, by which undue weight may be given to a secondary phase of a problem, or a generalization much wider than is justified be made. There is always a tendency to make too much of the new view.

A commendable feature of the book, although it may seem, at first, merely minor detail, is the symbol used for the factor of concentration. Sørensen, to whom is due so much of the development of the matter, introduced a symbol somewhat complicated in typographic form, and hence some difference is noted in the manner in which it is written and printed by different authorities. Leeds and Northrup, in a recent publication, use the original Sørensen form, but Clark uses the simpler form,  $P_H$ . This, also used by the *Journal of Biological Chemistry*, is much more easy for the compositor and fully as satisfactory to the chemist. There seems to be no reason for retaining a complex expression merely because it is the form originally suggested.

The procedures given in the book are wisely limited to the two types by which the concentration determinations are made in the working laboratory, that by indicators and that by electrometric methods. Both these methods are described in great detail. The theory of indicators has been the subject of extensive study among chemists, and the phenomena of color change under the differences of acidity and alkalinity are striking even to the experienced worker. The chemical and physical changes occurring in many indicators are complicated, involving even the reactions of tautomerism. Advance in the practical application of these substances has, however, brought out the fact that by the use of what are termed "buffer" solutions, indicators may be classed empirically, *i. e.*, without taking into consideration any theory. These buffer solutions are standard solutions of such well defined composition and hydrogen ion concentration that they can be accurately duplicated. For the highest accuracy, the degree of ion concentration should be verified by the electrometric method, which is an absolute one. They generally consist of a mixture of some acid and one of its alkali salts, Clark and Lubs have designed a set of these, the details of which

are given in the book. A double page color plate gives the range of tints resulting from different degrees of hydrogen ion concentration in action with a series of indicators of comparatively recent introduction and special adaptability to the problem in hand.

The book will be a great aid to the working chemist and especially to the bio-chemist. It is well printed, on good paper with good type and the literary merit is high, the language being clear and concise. An extensive bibliography and an account of many of the applications of the principle are added.

The book bears the statement "Published by the permission of the Secretary of Agriculture." Well, we suppose it is all right. Dr. Clark is a subordinate of that official, and presumably his work belongs to the government, and it is likely that the "permission" is mere routine, yet it does give the independent chemist a twinge to see the publication of such meritorious work even nominally dependent on an official who may not know anything about the matter.

HENRY LEFFMANN.

"A CRITICAL REVISION OF THE GENUS *EUCALYPTUS*." By J. H. Maiden, I.S.O., F.R.S., F.L.S., Government Botanist of New South Wales and Director of the Botanic Gardens, Sydney. Vol. V, Part 2.

This constitutes part XLII of the complete work, which we have reviewed from time to time as the parts have been received. The present contribution to this monographic study of the interesting Genus *Eucalyptus* covers the following species: *E. eximia* Schauer; *E. peltata* Benth; *E. Watsoniana* F. v. M.; *E. trachyphloia* F. v. M.; *E. hybrida* Maiden; *E. Kruseana* F. v. M.; *E. Dawsoni*; *R. T. Baker*; *E. polyanthemos* Schauer; *E. conica* Deane and Maiden; *E. concolor* Schauer.

The same style of description and excellence of illustrations that characterize the former parts of this voluminous study are exhibited in the part now before us.

G. M. B.

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# THE AMERICAN JOURNAL OF PHARMACY

DECEMBER, 1920

## EDITORIAL.

### WANTED—BOOSTERS FOR PHARMACY.

The columns of the current issues of some of the pharmaceutical journals again confirm the comment made by a non-interested observer that "much of the pharmaceutical literature of the day has a pessimistic tendency that is far from beneficial to the progress of pharmacy." In the past, we have expressed our opinion of the evil of disparagement<sup>1</sup> and the injury that pharmacy was sustaining from the continuous and deliberate "knocks" in print and public utterances and the disparagements appearing in "pharmaceutical journals." It is with chagrin and regret that we note another of these periodical storms of disparagement and observe that the showers are descending upon the American Pharmaceutical Association, our esteemed contemporary, *The Journal of the A. Ph. A.*, and the management thereof.

We take no exception whatever to any proper comment, objection, or even censure. On the contrary, we believe that constructive criticism is beneficial and on various occasions have exercised this right. There is, however, a wide disparity between fair and just criticism aimed to effect progress or a well thought out improvement and a distorted view that permits of such strange accusations as: "the policy under which the *Journal of the American Pharmaceutical Association* has been conducted for eight years is contrary to the wishes of 95 per cent. of the Association;" "that the prime object of the *Journal* as set forth in the initial declaration of the first editor was for the purpose of restricting its circulation, so that it shall circulate only among its active members;" "that it is worthless as an advertising medium;" "that there was a method in madness by which, in choosing the Committee on Publication, the

<sup>1</sup> Editorial—*A. J. P.*, April, 1919, p. 191.

editors of rival journals were preferred;" that a coterie has been in control of the journal and that these barnacles having about wrecked the ship are now yelling lustily for help."

This tissue of overdrawn, harsh and uncalled for accusations, it would seem had been penned during an attack of dyspepsia or a period of aberration that blotted from memory and barred from sight a more pleasing, characteristic and truthful picture. So absurd are these and other statements contained that refutation would appear as unnecessary. They must fall because of their lack of foundation, their inherent weakness and unbalanced construction. Unfortunately, despite the crumbling into the dust from which such mud pies are made, this derogation of the American Pharmaceutical Association and the aspersion of the motives of those who have so unstintingly devoted their best efforts to its upbuilding, remains as a vicious example of the disparagements emanating from some whose actions are not in harmony with their professed interest in the progress of pharmacy.

It is the duty of pharmacists to uphold the American Pharmaceutical Association and to sell membership therein to every druggist in America. Would any salesman commit such a suicidal act as to advertise to his prospective customers every possible defect or imaginary fault that either had occurred or that might arise in his merchandise.

All products of the human conception are prone to fall short of their ideals and this is but an evidence of the imperfection of man and the limits to his powers and knowledge wisely ordained by the Omnipotent and Omniscient Creator. The American Pharmaceutical Association is but the reflection of the imperfect endeavors of imperfect human beings to effect an ethical development of the commercial and professional aspects of pharmacy. Perfection cannot be expected and the faults of judgment and the errors of management are only the common experiences of all such organizations. In the past, we have frankly criticized some of these defects, however, without at any time questioning the sincerity or motives of its officers. We hold this as the common right of all members. The advocacy of any meritorious action does not require the disparagement of the great work of the Association and the honest endeavors of its active members. True reforms and actual progress are achieved through the orderly processes of evolution working along the paths of established forms and tried legal methods of procedure.

We have watched, with pride, the development of the American Pharmaceutical Association and have been pleased to note the continued extension of its activities in behalf of pharmacy. We firmly believe that these activities can be and will be further expanded as necessities or opportunities present themselves. We even venture the assertion that the further broadening out of its field of usefulness will be accomplished as a result of the sane deliberation of its conservative members and not through the propaganda of "knockers." The upbuilding will be continued on the bed rock of solid facts and accomplishments and not upon the illusionary shadows and day dreams of pessimists. "An ounce of up and doing is worth a pound of being done."

After all, the true measure of success is the service rendered, and this is directly in proportion to the adherence to the purposes of the organization. We wonder if these critics are acquainted with the history of the American Pharmaceutical Association and the spirit that has actuated the leaders thereof from its inception. The space available and likewise the purpose of this editorial will not permit us to present at this time the retrospect that we believe is necessary. However, we urge that the pharmacists give due consideration to the declared aims of the Association, its policies, its continual service in behalf of the advancement of both the scientific and the commercial sides of pharmacy, its research work, its attainments and its scientific publications.

Let each also give thought to what has been the influence of this Association upon his own career; the inspiration and the value of the example of the fathers of pharmacy who through its agency have added so much to the development of our vocation. Have we not cause for pride in their labors which now become our inheritance, and what a wonderful inheritance is ours. In turn, the present generation has the moral responsibility of upholding their ideals and traditions, of maintaining the faith, of continuing the upbuilding of the profession upon the sound principles that have been transmitted to us. Can one picture what would be the condition of pharmacy in America if the American Pharmaceutical Association had not been organized and ever since had not maintained its efforts for the advancement and protection of our calling?

The interests of pharmacy demand that the great body of American pharmacists should be brought into the membership of the A. Ph. A. and educated up to its standards and ideals and not that

these standards and ideals should be debased. Pharmacists must themselves establish and maintain the ethical status of their profession. This cannot be brought about by continuing to sow the apples of discord or the brambles of disparagement.

Equally unfortunate and disastrous to the profession is the attitude of those who favor extolling the position of other professions and decrying the status of pharmacy. The homely philosophy of Rastus' advice are words of wisdom for such:

"De sunflower ain't de daisy, and de melon ain't de rose;  
Why is dey all so crazy to be sumfin else dat grows?  
Jess stick to the place you're planted, and do the bes' you knows;  
Be de sunflower or de daisy, de melon or de rose."

Pharmacy has no mean inheritance, possesses a history worth extolling and many eminent devotees whose examples are worthy of emulation. The use of the hammer after all requires no great amount of intelligence, just physical strength. Is the "knocker" exercising even his strength to the best advantage? If pharmacy is to come into its own it must be by the very opposite method. The need of the time is for its boosting. Not by a few, but by all of those who claim to be within its ranks. G. M. B.

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## ISOTOPY.\*

BY HENRY LEFFMANN A.M., M.D.,

SPECIAL LECTURER ON RESEARCH, PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE.

The theory that matter is discontinuous and made up of minute particles which are incapable of diminution in mass or alteration in character, is of great antiquity. In fact, the word "atom" by which these particles are collectively designated, was coined by Greek philosophers many centuries ago, and the general principle stated that the properties of all substances depend on the nature of the atoms, the manner in which they are arranged and the motions they mutually impart and receive, phrases that sound much like those in

\*Abstract of an address delivered at a meeting of the Instructional Corps of the Philadelphia College of Pharmacy and Science.<sup>1</sup>

<sup>1</sup>The data for this communication are taken principally from a paper by Dr. Theodore W. Richards (*Science* [n. s.], 49: 1, 1919) and "Introduction a la Chimie Générale," by M. Copaux, a translation of which, by the author of this abstract is about to be published by P. Blakiston's Son & Co.



which modern chemists define their views of combination. The ancient Greeks must have reached their opinion by reasoning alone, for we have no indication that they carried out any experiments, and as they were substantially unfamiliar with the exact physical and chemical properties of gases, it does not seem possible that they could have applied inductive methods.

The atomic theory remained for many centuries unfruitful and merely a philosophic postulate. That it did not lead in Greece to a development of more definite data is probably, in part due to the idealism that overwhelmed the materialism of the early thinkers, but at any rate for many centuries the theory is not active in determining the course of investigation or thought.

In the early part of the nineteenth century, John Dalton propounded the theory in a definite form, and gave to the atom a quantitative relation that made it almost immediately a fundamental datum of chemistry and physics, a position which it has held without material modification until recent years. Dalton's claim to priority in the formulation of the modern atomic theory has been lately challenged by A. N. Meldrum, a Fellow of Bombay University, who, in a paper on "The Development of the Atomic Theory," asserts that William Higgins published substantially the same views about fourteen years before Dalton. This is not the place to discuss the question, but it is to be noted that the modern theory differs from the ancient one in the distinct quantitative relations that the several atoms bear to each other. In the same way the modern system of symbols differs from the earlier ones. The Greek alchemists of the early Christian centuries, had symbols for all the elements they knew, and methods of expressing certain classes of compounds, especially alloys, by associating the symbols, but Berzelius devised the system in which each symbol is not simply an abbreviation of the name of the element or derived from fanciful associations of it, but represents a definite weight in relation to a standard. A combination of the alchemistic signs for mercury and copper represents any proportion of those substances, but CuAg represents a definite proportion by weight.

The theory of the indivisibility and practical inalterability of the atom dominated the physical sciences for nearly a century, but is now materially modified, this modification having been brought about principally by the study of the phenomena of radio-activity. Space does not permit of description of the details of the methods of

research nor an extensive discussion of the present day views, but the following summary will suffice for an introduction to the special subject of this address.

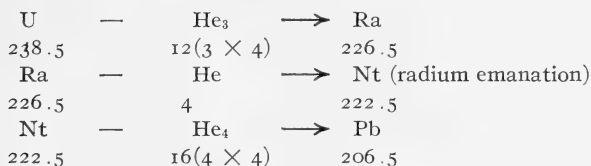
*The Electron.*—All atoms contain a common constituent, the electron, the discovery of which resulted especially from studies made with the Crookes tube. Differing completely from light, the cathode rays are made up of distinct corpuscles of extremely minute mass—about  $1/1700$  that of the atom of hydrogen—which corpuscles are negatively charged, and have a high velocity, approximating 50,000 kilometers per second. The velocity is dependent on the electric potential influencing them, but the charge and mass are always the same whatever may be the circumstances of their liberation. The electron, therefore, is a universal constituent of matter.

*The Positive Nucleus.*—To compensate for the negative charges of the electron, the neutral atom should contain a positively charged mass, which Rutherford considers as reduced to a very small central nucleus, about  $0.0001$  of the diameter of the whole atom. Around this positive nucleus, in which is concentrated the individuality of the atom and almost its whole mass, the electrons circulate in number about equal to half the atomic weight. Helium (at. wt. 4) has two electrons; carbon (at. wt. 12) has six, and so on, but hydrogen does not follow the rule as it has one electron and a positive nucleus. Moreover, though all electrons are identical among themselves, they probably do not have exactly the same value as constituent particles, for it seems illogical to suppose the same origin for the electrons that are emitted in such peculiar transformations as those of the radioactive substances (beta-rays), as the electrons that are concerned in the simple change of valency when ferrous salts are converted into ferric. In the former instance, the electrons probably come from a deeper and more essential part of the atom than do those in the latter.

It can also be assumed that the electrons are arranged in several concentric groups and be in close contact with the positive nucleus.

One of the results of this structure of the atom is the possibility of transformation of one type of atom into another, in other words, the creation of one element from another. This has been, as is well known, the dream of ages. It has now been shown to be possible, not along the lines in which the search has been made, namely, the conversion of the baser metals into gold, but in the conversion, for instance, of uranium into helium. It has been found that uranium

undergoes spontaneously slow conversion into radium, and that this conversion is accompanied by a liberation of three atoms of helium for every atom of radium produced. Radium further undergoes change by loss of one atom of helium, into a gas termed *niton* or *radium emanation*, and this emanation by loss of four atoms of helium, passes into a form of lead, which differs from lead extracted from the common ores by having a distinctly lower atomic weight. The sequence of change may be represented thus



Numerous, carefully made determinations of the atomic weight of lead from the ordinary ores (which are not radioactive) gave 207.2 as the average, but when the same determinations are made on lead from radioactive minerals, which always contain some lead, the atomic weight is, as shown above, sensibly lower.

An explanation that has been offered to account for phenomena of this type is that many of the common elements, if not all, are really made up of two or more closely accordant elements, agreeing in all or nearly all their chemical and physical properties, except slight differences in the atomic weights, and that the differing proportions in which such mixtures occur determine the slight variation in the atomic weights of the elements obtained from different sources. One difficulty in this view is to explain why in certain occurrences of the elements the proportions are always the same, since from such sources, the atomic weights are constant. It must be remembered, however, that the most striking instance of variability, that just set forth, relates to an element occurring under two distinctly different conditions, respectively with and without radioactive association. It must be borne in mind, by the way, that the lead obtained from radioactive ores is not itself radioactive. The emissive power ceases with the production of that element.

In consequence of these capacities of certain elements to change in atomic weight, several of them may be found in the same position in the periodic system, and for this reason they have been called "isotopes," from Greek words "equal" and "place."

An interesting feature of the phenomenon is that there is now exhibited in chemistry a disposition to return to the "whole number" theory of atomic weights. In 1815, Prout advanced the view that all elements are aggregations of the hydrogen atom, which is the lightest known, and hence all atomic weights should be whole numbers if referred to hydrogen as unity. This attractive supposition was soon rendered unacceptable by the researches of Dumas, Marignac and Stas, who showed that the most exact determinations of many atomic weights did not allow of the supposition of their being whole numbers. If, however, the duplex or multiple composition of the common forms of the elements is assumed, it may be, as noted above, that a mixture of two isotopes in certain proportions, though each has a whole number atomic ratio, will give a fractional ratio as compared with hydrogen. Thus, one of the most striking of fractional atomic weights is that of chlorine, the figure for which stands practically midway between two integers. Now if this element is a mixture of two isotopes, having respectively the atomic weights of 35 and 36, it is easy to see that in a certain proportion the mixture will yield a fractional ratio.

Isotopes are so far not separable by chemical means. In this respect, they constitute one step further in analogy to elements long known and separable. The known elements, although only a few score in number, present us with an epitome of the evolutionary relations of nature at large, just as the modern theory of atomic structure presents us with an epitome of the solar system, the nucleus with its more or less loosely held circulating electrons, resembling the sun with planets, moons, meteors, comets and cosmic dust tributary to it. Such elements as chlorine and potassium stand at the extremes of the series, their separation being almost automatic, then the members of the chlorine and potassium groups, respectively, agree closely among themselves, and their separation requires special care. Closer affiliations are noted between, for instance, nickel and cobalt, and still closer between the cerium metals, and, finally, the most recent specific separation of a supposed element into its constituents by chemical means is the decomposition of didymium into two distinct contrasting metals, neodymium and praseodymium, the former producing a series of bright red salts and the latter a series of brilliant green ones. The next problem of separation is that of the isotopes.

## THE THEORY OF PERCOLATION.

BY JAMES F. COUCH,

WASHINGTON, D. C.

(Continued from November number, page 796.)

### THE PERCOLATE.

The immediate product of percolation is the solution which issues from the percolator, the *percolate*. It represents a summation of the various complexes of the precolate and, to a certain extent, furnishes an index to the conditions within the apparatus. The changes which it undergoes are regular and have been the object of much careful study. There are, however, many questions involved which cannot, at present be answered and the whole subject needs revision and extension particularly since much of the study of percolates was made before the pharmacopoeial standard for fluidextracts was changed from a grain per minim to a gram per mil.

The first question which confronts us in this consideration is, what does the percolate represent? With our present knowledge this is exceedingly difficult, if not impossible, to answer. For such drugs as peppermint, ginger, or aspidium, which we percolate with a simple menstruum as alcohol or acetone, thereby dissolving but few of the constituents of the plant while the larger number of them is excluded, the lack of complexity of the precolate enables us to decide that the percolate represents that portion of the drug which is soluble in the given menstruum and the quantitative composition of the percolate bears a direct and simple relation to the degree of exhaustion and composition of the partially exhausted drug then in the percolator.

When, however, we are dealing with drugs of more complex composition, and are extracting them with a complex solvent such as diluted alcohol, the strength of which, and consequently its solvent powers, is variable the answer to the question is not so easy to formulate. As I have fully outlined above, the composition of the precolate is variable under such circumstances, the qualitative composition of the drug varies in different parts of the percolator through physical reactions and, as a result the percolate represents a summation of the conditions within the percolator some of which are mathematically negative and none of which have been satisfactorily investigated. A percolate collected in such a case will vary in the composition of its different parts and this variation will be not only quantitative but qualitative and may lead to precipitation on mixing.<sup>1</sup>

<sup>1</sup> Cf. Lloyd, *Proc. A. Ph.* 1881, 408.

The composition of the percolate depends upon several factors; the nature of the drug, the condition of the drug, the nature of the menstruum, the shape of the percolator, the manner in which the drug is packed in the percolator, and the rate at which the percolate is allowed to flow from the apparatus.

The first five factors have already been considered; the last may profitably engage our attention now. All pharmacists who have devoted time to the study of percolation have recommended that the flow of percolate be retarded to a very slow dripping. Squibb<sup>1</sup> says: "It is an axiom in percolation that the slower it is performed the more perfect and sudden is the exhaustion, and with the smallest quantity of menstruum." Again, for percolating one pound of drug he directs a rate of flow of one drop every two seconds or "about 3 fl. oz. per hour; and for larger quantities in the same ratio."<sup>2</sup> Bedford<sup>3</sup> agrees with this but adds that the rate of flow may be increased toward the end of the percolation. This latter idea as I shall presently show, is erroneous. Lloyd<sup>4</sup> and Procter<sup>5</sup> have also declared in favor of slow percolation.

How slow should we percolate? Obviously the criterion is the strength of the solution which issues from the apparatus; we should control the rate of flow just as we control the time of maceration, that is, in such a way as to obtain as concentrated a percolate as is desirable, not necessarily as concentrated as possible. For we may, by disregarding the time consumed, keep increasing the strength of our percolate at the expense of time, though at a diminishing rate, apparently for months. Time, however, cannot be neglected for it is one of the most important factors pharmaceutically and financially. The time, therefore, which we can allow for the obtaining of a certain amount of percolate is limited and must be gauged, like the time given to maceration, by the operator's experience and judgment.

Squibb allows a faster rate of flow, "in the same proportion," for large quantities of drug. This is open to some further consideration for, as I have already pointed out, it is not practicable to use as fine a powder of certain drugs in large quantities, enough

<sup>1</sup> This Journal, Vol. 39, 400, (1867).

<sup>2</sup> This Journal, Vol. 30, 97, (1858).

<sup>3</sup> *Pharm. Record*, 6, 19, (1886).

<sup>4</sup> *Proc. A. Ph. A.* 1879, 682.

<sup>5</sup> *Pharm. Jour.* 19, 139, (1859).

to prepare ten or twenty-five gallons of fluidextract for instance, as one may use in the much smaller pharmacopoeial amounts, and it is my opinion that, the coarser the drug, the slower should be the rate of flow of percolate.

The time factor will materially influence the rate at which the percolate changes from a nearly saturated solution to nearly pure menstruum so that no mathematical rule which does not take it into consideration can be applied to the variation in the composition of the percolate. We may, however, state in general terms the character of this variation and present a definite idea of the phenomena involved.

*Specific Gravity.*—The first portions of percolate are laden with extracted matter and are specifically heavier than any succeeding fraction. They may, indeed, present a greater specific gravity than the fluidextract made from the drug due to the fact that they may contain not only more extract but a larger proportion of water which originates in the natural moisture of the drug. If the fractions of percolate are taken in small volumes it may be found that the second fraction is of greater specific gravity than the first due to an actually greater content of extract.<sup>1</sup> As above suggested this anomalous condition is probably due to the first portion of percolate lying during the larger part of the maceration quite out of contact with the drug.

The lowest specific gravity possible is, of course, that of the menstruum and this is the limit which the changing values for the fractions approach. It has been found<sup>2</sup> that the character of the change in the specific gravity of successive fractions as percolation proceeds is quite regular and furnishes a rough indication of the degree to which the drug has been exhausted.

Accompanying the change in specific gravity we find a decrease in the amount of extract contained in the individual fractions, each being a little less concentrated than its immediate predecessor. If the percolation has not been interrupted so that no period of maceration has occurred since the start of flow of percolate, the decrease of extract concentration proceeds with regularity as the following table, taken from one of Lloyd's publications,<sup>1</sup> shows.

<sup>1</sup> Lloyd, *This Journal*, Vol. 50, 434, (1878).

<sup>2</sup> Squibb, *This Journal*, Vol. 50, 229, 223, (1878).

TABLE I.

Percolation of 7680 Grains of *Cimicifuga*.

Fluidounce of Percolate.	Gms. of Dry Extract.	Fluidounce of Percolate.	Gms. of Dry Extract.
1	3.33	13	0.77
2	2.80	14	0.68
3	2.38	15	0.58
4	2.19	16	0.35
5	1.94	17	0.36
6	1.71	18	0.32
7	1.43	19	0.23
8	1.34	20	0.22
9	1.12	21	0.22
10	0.84	22	0.21
11	0.79	23	0.22
12	0.73	24	0.21

These results have been plotted as Chart B and show in a striking manner the uniformity of the decreasing extract content in the percolate. Many similar results from the work of Squibb, Diehl, Robbins and others confirm the fact of regularity in extraction.

When, however, we subject the experimental results to mathematical treatment we discover no expression which applies to the conditions of every fraction. Instead, in the case of every formula which one would expect to generalize the phenomena, we find variation where we should obtain constancy, and, furthermore, the variation appears to proceed in a regular fashion from one fraction of the percolate to the next equal fraction, either increasing or decreasing the "constant," which indicates that a constantly varying factor or set of factors is missing from our data.

What these missing factors are can only be indicated here. I hope to consider this phase of the subject more in detail at some future time when I may present new data. The first factor which may vary is the chemical composition of the extract contained in each fraction. From the evidence presented under the discussion of the composition of the percolate we should expect the first fractions of the percolate to differ qualitatively from those fractions obtained toward the end of the process. This question was investigated by Squibb on cinchona<sup>1</sup> and on podophyllum.<sup>2</sup> He states: "The extract or soluble matter yielded to the menstruum is not

<sup>1</sup> This Journal, Vol. 39, 402, (1867).

<sup>2</sup> This Journal, Vol. 40, 1, (1868).



uniform in its chemical and therapeutical value as obtained during the different stages of the percolation, but diminishes in effective value far more rapidly than the extract does in weight." In support of this statement he reports experimental results showing the

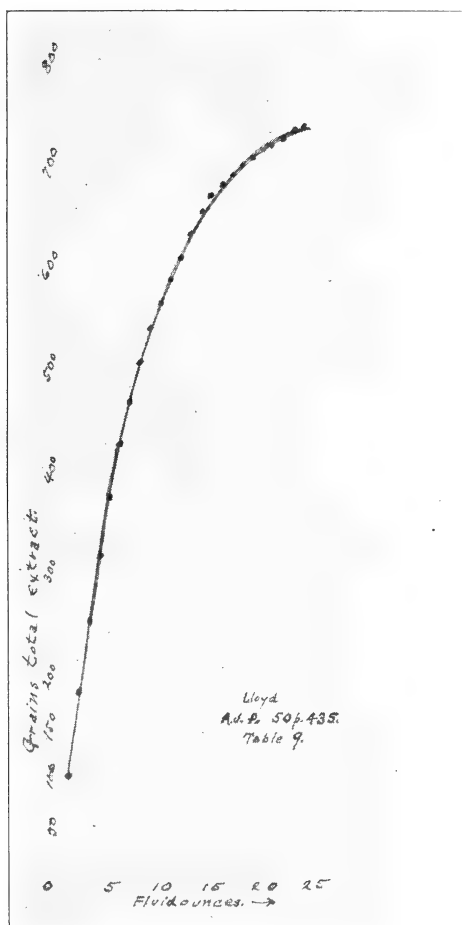


Chart B.

weight of total extract obtained from fraction of a percolate and its content of some active material. These results show conclusively that there is a great difference in the rate at which the various soluble matters of a drug are extracted by the menstruum, and, in the cases which Squibb chose, the pharmacologically important substances

were extracted more rapidly than the inert compounds so that the first portions of the percolate contained a larger percentage of the alkaloids or resin than the total extract. Squibb's<sup>1</sup> results are plotted as Charts C and D and plainly show the phenomenon. Lloyd

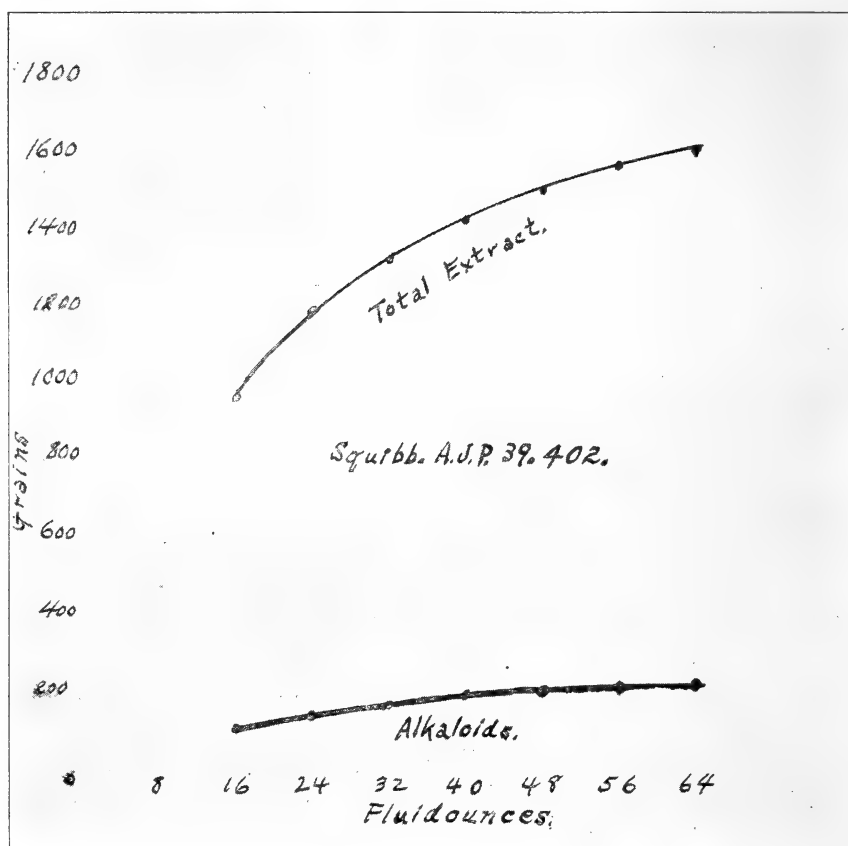


Chart C.

has confirmed this observation by several experiments, notably upon cannabis and cascara.<sup>2</sup>

A second variable factor may arise if menstrua of certain types are employed. These types of menstrua include hydro-alcoholic, glycerinated, and acidulated menstrua. It frequently happens that

<sup>1</sup> This Journal, Vol. 38, 109, (1866.) Vol. 39, 289, 402, (1867).

<sup>2</sup> Proc. A. Ph. A. 1881, 408.

the relative proportion of the mixed solvents is not the same in the liquid portion of the percolate as it is in the menstruum and for the following reasons: where acids or glycerin are added to the menstruum the addition is frequently made wholly to the first portions used to moisten the drug so that the bulk of the component is found in the primary fractions of the percolate. With hydro-alcoholic menstrua, which do not usually vary to any great extent throughout the process, other conditions arise which may alter the proportions of alcohol and water found in the percolate.

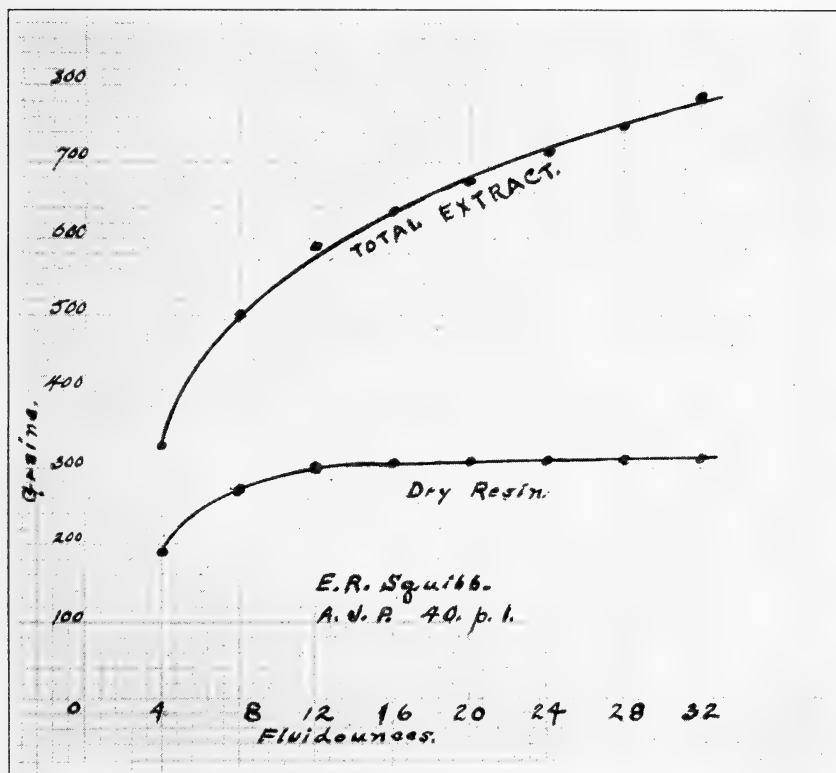


Chart D.

In the first place given a menstruum of high alcoholic content, the first portions of the percolate will contain most of the water which the drug originally held as moisture. This usually averages from six to ten per cent. of the weight of the drug and such a comparatively

large amount of water concentrated in a small volume must materially affect the alcoholic strength of the solvent. Conversely, a fibrous drug will actually absorb water from a menstruum of low alcohol content so that the first portions of the percolate will contain a solvent of higher alcoholic strength than the original menstruum. It is, perhaps, unnecessary to comment upon the possibility that conditions of this sort are almost certain to lead to extensive precipitation in liquid products.

The actual alcoholic strength of the percolate increases in every percolation as the content of extract diminishes and the volume of solvent becomes greater. There has not been, up to the present time, any published determination which shows the regularity of this increase in alcoholic percentage but the fact is well known if too often disregarded. Lloyd has suggested that the solvent power of a partially saturated menstruum is qualitatively different from that of the fresh menstruum; it would be of considerable interest in connection with the problems of percolation if this question were fully investigated.

#### THE MARC.

With the exhaustion of the drug the process of percolation enters a new phase. The residue within the percolator, however, may still claim attention for it usually contains a quantity of valuable material, especially alcohol. The recovery of this valuable substance properly belongs to the economic side of the process and is highly important. A variety of methods are used for this purpose: the most common procedure and the one which is always applied in large scale operations is the use of a dreg still into which the wet marc is packed and then subjected to the action of live steam which drives off nearly all the alcohol in vapor and this is then condensed by suitable means and collected. About two-thirds of the residual menstruum may be recovered by pressing out the marc in a tincture press but this is neither convenient nor economical for large operations. Washing out or "displacing" the menstruum with water is the process first used by pharmacists<sup>1</sup> to recover the valuable alcohol. Smith<sup>2</sup> has described a percolator which has an ingenious device whereby the apparatus may be reversed and the alcohol floated out of the

<sup>1</sup> *Jour. de Pharm.* 2, 165, 468, (1816). This Journal, Vol. 91, 17, (1919).

<sup>2</sup> *Pharm. Jour.* 18, 291, (1858).

marc on water introduced below and Elborne<sup>1</sup> later advocated the same idea.

As early as 1836, however, the use of water to "displace" alcohol from marcs was questioned by Soubeiran<sup>2</sup> who showed that, contrary to the earlier idea, the displacing water mixes with the alcohol of the menstruum. Indeed it is doubtful whether much more than three-fourths of the residual alcohol can be recovered by this process, for the quantity of water necessary even to approximate a complete washing out of the menstruum is impracticably great and the last portions are too weak in alcohol to allow economical handling. The following case, from the writer's experience, will serve as an illustration. Twelve pounds of coarsely ground drug were moistened, packed, and percolated in the usual way with twelve gallons of diluted alcohol. When the percolator had drained the residual menstruum was displaced with water and the issuing liquid tested from time to time for the presence of alcohol. After thirty gallons of water had passed through the marc the next portion of liquid gave strong evidence of the presence of alcohol. It may be somewhat roughly calculated that, at the end of the percolation, the marc contained six pints of alcohol and that, therefore, forty times its volume of water was insufficient to wash it completely from the drug fibre. In addition to its general inefficiency the practise of washing alcohol out with water is not applicable to mucilaginous drugs like senna, buchu, gentian, or rhubarb which form a gelatinous mass within the percolator as soon as a portion of the alcohol has been removed and this effectually terminates the process.

#### HOT PERCOLATION.

It is usually possible to hasten the process of percolation by employing a hot menstruum and several forms of apparatus have been devised for this purpose. In general this procedure offers no advantages over the ordinary cold process except shortening the time. Hot solvents, too, frequently dissolve substances which are insoluble in the cold solvent and which are deposited with more or less promptness as soon as the percolate reaches the room-temperature. Alcohol, for instance, dissolves saponins, waxes, hydrocarbons, and phytosterols when hot and deposits them on

<sup>1</sup> *New Remedies*, 9, 323, (1880); from *Pharm. Jour.*

<sup>2</sup> This Journal, Vol. 10, 221, (1838); from *Bul. Gen. de Therapie*.

cooling. If the deposit occurs soon after the percolation the case is sufficiently undesirable but if the insoluble matter does not precipitate for some time or if the deposition is spread over a long period of time it makes an unsightly product which does not redound to the pharmacist's credit.

Percolation with hot water, as, for instance, in the extraction of cascara and of triticum, is commendable and desirable for, with cold water which percolates very slowly and which contains nothing of a preservative nature, molds are quite likely to develop in the wet drug which renders the product unfit for medicinal use.

#### OTHER METHODS OF PERCOLATION.

One of the prominent characteristics of pharmacists as a class is their ingenuity and this is nowhere more apparent than in the number and extent of the processes which they have devised in the last hundred years for extracting drugs. Since the early apparatus of Count Réal<sup>1</sup> which was the first step in the abolition of the use of the tincture press down to the present time new forms of apparatus and novel methods for percolation have appeared in a continuous stream.

In the case of most of these novelties the words of John U. Lloyd apply with significance, "simple percolation is as yet unexcelled and my experience with complex forms of apparatus has invariably led to their rejection and a return to the simple percolator."<sup>2</sup>

It is my purpose here to consider in detail first the processes which have been applied most widely and then to refer briefly to the less common methods.

#### REPERCOLATION.

When the price of alcohol rose following the disturbed conditions incident to the Civil War it profoundly affected pharmaceutical practise. Dr. Squibb set himself to the task of finding some method for economizing the use of alcohol in percolation. His first suggestion was that instead of using a large volume of alcohol to extract the weaker portion of a partly exhausted drug, the weak drug should be sacrificed and the alcohol saved, the pharmacist being satisfied with 75 per cent. of fluidextract from 100 parts of drug.<sup>3</sup> Later<sup>4</sup> a similar suggestion was made by F. B. Stuart.

<sup>1</sup> *Jour. de Pharm.* 2, 165, (1816).

<sup>2</sup> *Proc. A. Ph. A.* 1887, 582.

<sup>3</sup> *Proc. A. Ph. A.* 1865, 201.

<sup>4</sup> *Proc. A. Ph. A.* 1888, 250.

This idea was not favorably received however, and, in the next year,<sup>1</sup> Squibb published the details of his process of repercolation, "Improved Process for Official Fluid Extract of Buchu," following it with an application to cinchona<sup>2</sup> and, much later, with an extensive study which may well be considered a pharmaceutical classic.<sup>3</sup> In the earlier directions for his process Squibb adopted the customary evaporation of weak percolate; later he revised the procedure so that a fluidextract was obtained directly from the process without evaporating and the weak percolates were preserved and used on the next batch of drug.



DR. E. R. SQUIBB

Originator of the process of repercolation.

At about the same time a similar process was developed in England by R. W. Giles.<sup>4</sup>

The fundamental principle of repercolation is to saturate thoroughly the first fractions of percolate by mixing them as macerating menstruum with fresh portions of the drug. In the revised process, the drug is divided into three or four portions which may be of equal weight or which may decrease in weight from the first to the last to be treated; the first portion is percolated in the ordinary fashion and a definite amount of percolate reserved; a second

<sup>1</sup> *Proc. A. Ph. A.* 1866, 81.

<sup>2</sup> *Proc. A. Ph. A.* 1867, 391.

<sup>3</sup> This Journal, Vol. 50, 209, (1878). *Ephemeris*, 3, 993, (1887).

<sup>4</sup> *Pharm. Jour.* 26, 219, (1866); 33, 521, (1873). *Proc. A. Ph. A.* 1867, 140,

definite amount of percolate is taken and this is used to moisten the second quantity of drug. The remainder of the percolate from the first portion is used to percolate the second quantity of drug. A definite volume of percolate from this second percolation is reserved, the next fraction of percolate used to moisten the third lot of drug, and the rest used to percolate the third lot. The percolate from the third quantity of drug is handled exactly as that from the

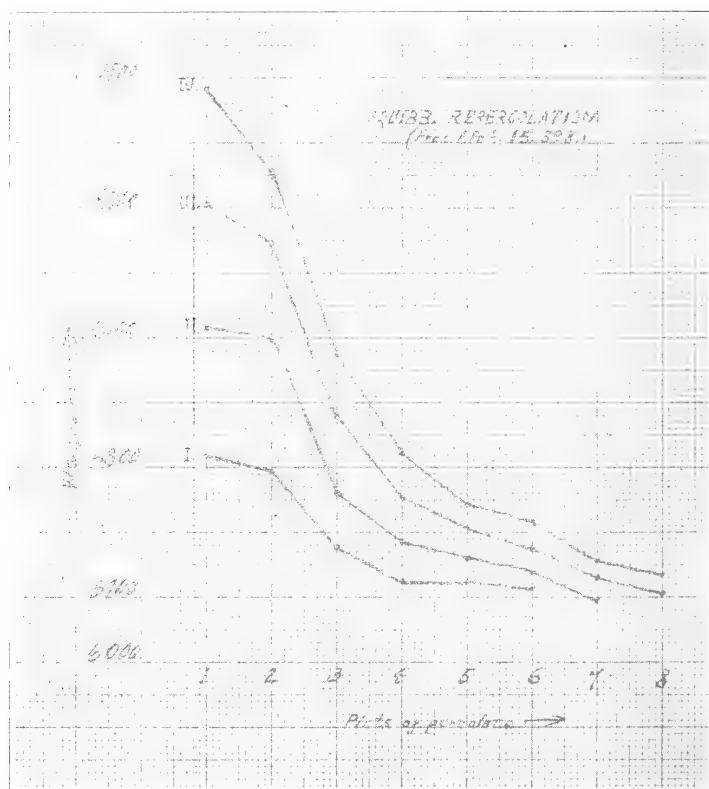


Chart E.

first and second lots and so with the fourth fraction when all the reserved portions are mixed together and used as finished fluidextract the weak percolates from the last percolator being set aside for the next extraction of the particular drug.

Chart E. presents in graphic form the results reported by Squibb in the repercolation of red cinchona by his first process. Four por-



tions of sixteen troy ounces each of drug were extracted in succession; the percolate was collected in fractions of a pint each and weighed. As pint No. 1 from percolation No. 1 becomes approximately pint No. 2 from percolation No. 2 and pint No. 3 from percolation No. 3, etc., the difference in weight between the pints shows the increased saturation due to Squibb's method.

This ingenious process has been subjected to detailed study by many investigators and has provoked much discussion and criticism. Procter<sup>1</sup> protested that the complicated manipulation involved in the process made it unsuitable for the pharmacopoeia. Diehl,<sup>2</sup> who termed it "fractional" percolation, made an extensive study of it with the coöperation of several other pharmacists. He concluded that fractional percolation offers no advantages over the simpler process. The following figures taken from one of Diehl's tables shows the percentage of the total extract which was contained in the reserved portion in the two processes of simple and fractional percolation:

Drug.	Simple.	Fractional.
Taraxacum,	66.43 per cent.	75.00 per cent.
"	83.75 "	82.51 "
Senna leaves	67.95 "	
"	66.80 "	72.79 "
Eucalyptus leaves	62.50 "	75.32 "

Lloyd<sup>3</sup> decided in favor of simple percolation after extensive experimentation; Moore's results show only a slight advantage in repercolation;<sup>4</sup> Army and Oxley<sup>5</sup> found simple percolation better for gentian; Kelley<sup>6</sup> did not find repercolation satisfactory for gentian, uva ursi, or squill; and Sayre reported it insufficient.<sup>7</sup>

J. W. Colcord, after wide experience with various forms of percolators, concluded that repercolation must ultimately become the official process.<sup>8</sup> Andrews<sup>9</sup> found a slightly modified repercolation

<sup>1</sup> This Journal, Vol. 41, 295, (1869).

<sup>2</sup> *Proc. A. Ph.A.* 1879, 727; 1880, 424; 1878, 681; This Journal, Vol. 41, 337, (1869); *Pharm. Rund.* 7, 25, 60, (1889).

<sup>3</sup> This Journal, Vol. 50, 12, (1878).

<sup>4</sup> This Journal, Vol. 62, 333, (1890).

<sup>5</sup> *Proc. A. Ph. A.* 1910, 1104.

<sup>6</sup> *Proc. Kansas Ph. A.* 1897, 15; *Proc. A. Ph. A.* 46, 683, (1898).

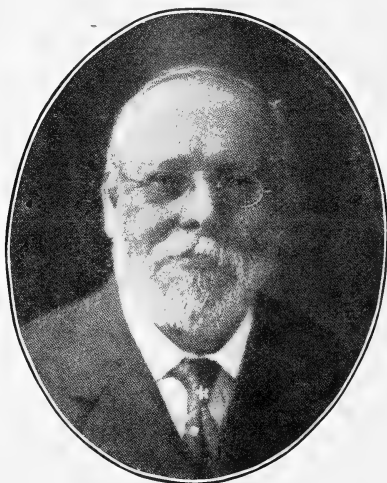
<sup>7</sup> *Drug. Circ.* 1897, 212; *Proc. A. Ph. A.* 1898, 685.

<sup>8</sup> *Proc. Mass. Ph. A.* 5, 170, (1886); *Proc. A. Ph. A.* 1887, 10.

<sup>9</sup> *Pharm. Jour.* 68, 336, (1902).

process suitable for the extraction of alkaloid drugs. Bird<sup>1</sup> approved of the process and Musset<sup>2</sup> recommended repercolation for the preparation of fluidextracts. Scoville<sup>3</sup> stated that repercolation is satisfactory for the extraction of resinous drugs.

In expert hands the process of Squibb gives excellent results with menstrua which do not contain a large proportion of water. In the extraction of those drugs which, like gentian, rhubarb, kino, and phytolacca, yield large quantities of extractive soluble in diluted alcohol the simpler process is preferable but repercolation may



PROF. C. LEWIS DIEHL

A painstaking worker on fluidextracts and the processes of percolation.

be applied to advantage in the extraction of ginger, cimicifuga, ergot, hydrastis, gelsemium, and especially where such solvents as acetone, chloroform, ether, or ligroin are used as menstrua.

#### INTERRUPTED PERCOLATION.

Interrupted or suspended percolation is the name given to a variation of the ordinary process of simple percolation by C. A. Seifert.<sup>4</sup> The practise in this case is founded upon sound principles

<sup>1</sup> *Pharm. Jour.* 54, 158, (1894).

<sup>2</sup> *Pharm. Centr.* 1897, 862; *Proc. A. Ph. A.* 1898, 681.

<sup>3</sup> *Proc. A. Ph. A.* 1910, 1114. (Discussion.)

<sup>4</sup> *Proc. Calif. Ph. A.* 1892, 123.

and has been approved by many students of extraction. It is based upon the idea of combining maceration with percolation in such a way that every portion of fresh menstruum added to a drug in a percolator shall have as much or more opportunity to macerate the drug as the first portion of menstruum has under the official procedure. As is well known, the early portions of percolate contain the most readily soluble constituents of the drug so that the later fractions of the menstruum encounter the most difficult portions of the extractive to dissolve. The common idea seems to be that the rate of flow of percolate may be accelerated as the percolation proceeds inasmuch as the quantity of extractive is diminishing and therefore does not require as long for solution, whereas the converse is really the true condition.

The principle of interrupted percolation is as follows: The drug is moistened and packed in the usual way and is then macerated for the official period with enough menstruum to "flood it;" at the termination of the period of maceration percolation is begun and a quantity of percolate equivalent to the volume of menstruum first added is collected. Meanwhile fresh menstruum has been added to take the place of that percolated out and, when the first volume of percolate has been obtained, the percolation is stopped and the drug allowed to macerate in the second portion of menstruum. After a certain time percolation is again allowed to proceed until the second menstruum has been percolated out, a third portion of fresh menstruum having been added to the drug. The percolation is again stopped, the drug again macerated, and the procedure continued until the drug is exhausted.

Searby<sup>1</sup> strongly approved this method as also did Edel<sup>2</sup> who claims that the reserved portion in the manufacture of fluidextracts by this method contains more extract than that in the U. S. P. process. J. W. Colcord<sup>3</sup> was also of the belief that alternate maceration and percolation is the best procedure for the extraction of a drug. Seifert shows that interrupted percolation is of especial value with drugs which yield large amounts of extract, as senna or cinchona. With resinous drugs such as ginger, the process did not present any advantage over simple percolation. Seifert reports the following results.

<sup>1</sup> Discussion, *Proc. Calif. Ph. A.* 1892, 125.

<sup>2</sup> *West. Drug.* 1893, 218; 1899, 216.

<sup>3</sup> *Pharm. Rec.* 6, 197, (1886).

TABLE.

		Senna.		Cinchona.		Ginger.	
		S. G.	Per Cent.	S. G.	Per Cent.	S. G.	Per Cent.
Fraction	1	1.025	15.00	0.952	11.66	0.885	25.00
"	2	1.050	22.50	0.976	26.66	0.050	7.50
"	3	1.044	20.00	0.994	28.33	0.842	3.33
"	4	1.036	20.00	1.020	38.00	0.836	1.66
"	5	1.018	16.00	1.010	31.66	0.827	0.83
Finished Fldext.		1.035	18.00	1.000	26.66	0.846	6.66

Seifert does not state the quantities of drug taken nor the volume of percolate collected but inspection of his paper leads to the opinion that he used 1,000 Gms. of drug and collected 200 Mil. portions of percolate. He suspended the percolation for 24 hours between the collection of each fraction of percolate and did not vary this period during the process. His results plainly show the advantages of alternate periods of maceration and percolation.

Many years earlier Alonzo Robbins<sup>1</sup> investigated the effect of interrupting percolation in connection with some other work and his results led him to conclude that no advantage came of it. Robbins, however, did not give the method a fair trial; he shortened the period of maceration as the time went on instead of lengthening it or keeping it uniform and also abandoned the macerating after four periods of maceration. Nevertheless a critical scrutiny of his results show a slight advantage in the interrupted process.

In the same year Lloyd<sup>2</sup> published the results of an experiment on the extraction of *cimicifuga* by what he termed "interrupted" percolation, proceeding as follows: 24 troy ounces of drug were moistened and packed and, without macerating one fluidounce of percolate was run off. The operation was then suspended and the drug was allowed to macerate for sixteen hours at 100° F. Then seven portions of one fluidounce each were percolated off. The drug was again macerated one day and eight fluidounce portions of percolate were collected. After 32 fractions had been collected the percolate was taken in two-ounce fractions until the drug was exhausted. Results from this experiment are plotted in Chart F. This experiment clearly shows the increased concentration due to the maceration. The idea of combining maceration with percolation was apparently favored also by Squibb for, in

<sup>1</sup> This Journal, Vol. 50, 329, (1878).

<sup>2</sup> This Journal, Vol. 50, 437, (1878).

his description of the well-tube percolator, he says<sup>1</sup> one of the advantages of the apparatus is that it combines maceration with percolation.

In this connection some figures obtained by the writer in the

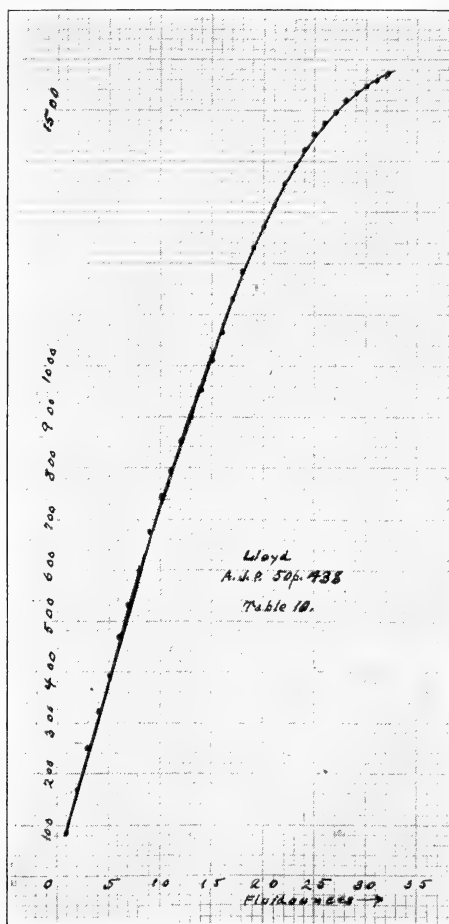


Chart F.

extraction of 16  $\frac{2}{3}$  pounds of phytolacca are of interest. The drug was moistened, packed in the usual way and macerated with diluted alcohol for two days. Three pints of percolate were then taken, the flow being adjusted to drops. The percolator was shut

<sup>1</sup> *Proc. A. Ph. A.* 1872, 183.

and the drug macerated for four days at the end of which time three pints more of percolate were collected. Then the drug was macerated for six days when a third three pints were collected; the next maceration was for eight days at the end of which time three pints of percolate were run out. The last period of maceration was ten days long and then four pints of percolate were collected. The specific gravities only of the percolates were determined. Below is a tabulation of the results:

TABLE.

Fraction.	Period of Maceration.	Specific Gravity.
1	2 days	0.9853 at 25° C.
2	4 "	0.9848
3	6 "	0.9833
4	8 "	0.9826
5	10 "	0.9657

The specific gravities of the first four percolates were almost identical and this shows a distinct advantage in the process especially when it is remembered that the first portions of percolate usually contain all of the drug moisture and so are of higher specific gravity than equally concentrated solutions, the solvent of which is the undiluted menstruum. The above process occupied 30 days which, it may reasonably be argued, is too long a time to devote to a percolation of this sort. But if one considers the economy of menstruum, the elimination of many details of the other processes, and the quality of the product, this process must be recommended as practicable. At present the writer is using it exclusively in extensive work on the extraction of plants and finds it satisfactory.

#### METHODS INVOLVING THE USE OF PRESSURE.

From time to time it has been considered advisable for a variety of reasons to hasten the rate at which the precolate passes through the drug by applying extra pressure to the percolation apparatus. A large number of ingenious forms of apparatus have been devised to carry out this purpose. They may be classified in three ways according to the manner of applying the extra pressure. The first class follows the method of Count Réal<sup>1</sup> who contrived a tall column of liquid so that the hydrostatic pressure would act directly upon the surface of the packed drug and some of this class are

<sup>1</sup> *Jour. de Pharm.* 2, 165, (1816).

merely modifications of Réal's apparatus. In this category belong the methods of Wuertzer,<sup>1</sup> Brandes,<sup>2</sup> Beindorf,<sup>3</sup> Rosenwasser,<sup>4</sup> Berry,<sup>5</sup> Hallberg's peerless percolator,<sup>6</sup> A. I. Cohen,<sup>7</sup> and of B. S. Procter.<sup>8</sup>

A second class utilizes air pressure applied to the surface of the drug. Pumps of various kinds are employed by Semelbauer,<sup>9</sup> in three forms of apparatus suggested by Romershausen,<sup>10</sup> by Signoret,<sup>11</sup> Allen,<sup>12</sup> Nunn,<sup>13</sup> and by Lenz.<sup>14</sup> Marpmann,<sup>15</sup> Phillips,<sup>16</sup> and Cowley<sup>17</sup> utilize air pressure obtained by the force of a column of liquid acting on an enclosed volume of air. The elaborate method of Duffield,<sup>18</sup> Fairthorne,<sup>19</sup> and Thompson,<sup>20</sup> include exhaustion of the drug, vacuum maceration, and expulsion of the percolate by compressed air.

The third class accomplishes the pressure by applying suction to the bottom of the percolator. Maben<sup>21</sup> employs an ordinary water pump or aspirator; Arthur<sup>22</sup> uses an exhausting syringe, and Platt<sup>23</sup> a Sprengel pump.

It must be borne in mind that any process which employs pressure other than that produced by the natural effect of gravity upon the menstruum is not a true process of simple percolation because

<sup>1</sup> *Rep. der Pharm.* 7, 230, (1819).

<sup>2</sup> *Ibid.* 7, 234, (1819).

<sup>3</sup> *Mag. für d. Pharm.* 9, 185, (1826).

<sup>4</sup> This Journal, Vol. 53, 567, (1881).

<sup>5</sup> This Journal, Vol. 55, 587, (1883).

<sup>6</sup> *West. Drug.* 15, 46, (1893); *Proc. A. Ph. A.* 1893, 383.

<sup>7</sup> Merck's Report, 1899, 4; *Proc. A. Ph. A.* 1899, 383.

<sup>8</sup> *Pharm. Jour.* 36, 641, (1877); This Journal, Vol. 49, 372, (1877).

<sup>9</sup> *Rep. der Pharm.* 3, 88, (1817).

<sup>10</sup> *Ibid.* 6, 316, (1819).

<sup>11</sup> This Journal, Vol. 33, 319, (1861).

<sup>12</sup> *Pharm. Rec.* 7, 6, 66, (1887).

<sup>13</sup> *Pharm. Jour.* 1898, 981.

<sup>14</sup> *Ber. d.d. Pharm. Ges.* 15, 137, (1905).

<sup>15</sup> *Pharm. Centr.* 29, 507, (1888).

<sup>16</sup> *Pharm. Rec.* 8, 213, (1888).

<sup>17</sup> *Pharm. Jour.* 1898, 418.

<sup>18</sup> This Journal, Vol. 41, 2, (1869).

<sup>19</sup> This Journal, Vol. 54, 236, (1882).

<sup>20</sup> This Journal, Vol. 55, 537, (1883).

<sup>21</sup> *Pharm. Jour.* 46, 941, (1887).

<sup>22</sup> *Pharm. Jour.* 49, 850, (1889).

<sup>23</sup> *Pharm. Era*, 1892, 113; *Proc. A. Ph. A.* 1892, 403.

the relationships between the drug, absorbed menstruum, and the precolate are upset when the precolate is driven through the drug. If a drug is suitable for extraction by simple percolation, then a proper regard for the conditions of fineness of powder, moistening, packing, and choice of menstruum will be sufficient to ensure success without any resort to external force. As I have shown above, the idea that the precolate may be hastened through the drug is based upon erroneous notions of the principles of percolation. The ideal condition is such a one that the menstruum is in contact with the drug just long enough to establish equilibrium between the factors present before the liquid drops through the orifice. This equilibrium is not established in any short period of time and, consequently, any process which does not take this idea into consideration is open to pharmaceutical objection. These complex forms of apparatus have uniformly been rejected by pharmacists and the simple percolator still is to be seen in every establishment where drugs are extracted.

#### MISCELLANEOUS PROCESSES AND APPARATUS.

The following contains a brief chronological account of a number of processes for percolating drugs and making fluidextracts with an indication of the essential feature of each.

The well-tube percolator of Squibb has already been described. The same idea is used in a percolator made of "Appert" glass.<sup>1</sup> Squibb has also described<sup>2</sup> an "automatic" percolator the chief feature of which is an ingenious method for the automatic addition of menstruum to the drug.

In 1858 appeared Bashford's Compound Percolator which is provided with an outside jacket so that it may be operated to allow hot percolation.<sup>3</sup>

N. S. Thomas<sup>4</sup> in 1865 obtained a patent for a method of preparing fluidextracts which consists in moistening the drug with successive portions of the menstruum, macerating, and pressing out in a tincture press after each addition. The operation is continued until the amount of liquid pressed out is equal in volume to the fluidextract which the given amount of drug should furnish. Squibb<sup>5</sup> says the process is an old one.

<sup>1</sup> Remington, "Practice of Pharmacy," 1907, 375.

<sup>2</sup> This Journal, Vol. 30, 97, (1858).

<sup>3</sup> This Journal, Vol. 30, 81, (1858); from the *San Francisco Bulletin*.

<sup>4</sup> This Journal, Vol. 37, 81, (1865).

<sup>5</sup> This Journal, Vol. 37, 182, (1865).



Dursse<sup>1</sup> patented a percolator with a tightly fitting cover which may be adjusted to control the rate of flow of percolate and which minimizes evaporation.

In 1869 Samuel Campbell published his process for the preparation of fluidextracts.<sup>2</sup> Campbell believed maceration to be the most important part of percolation. He used glycerin in his menstrua and macerated the drug for four days after packing it in a glass funnel percolator. After the maceration the drug was percolated until the proper volume of fluidextract was obtained when the operation was stopped and the percolate treated as finished fluidextract. This did away with prolonged percolation to obtain weak percolates which must be concentrated and dissolved in a reserved portion. But Campbell's process did not thoroughly extract the drug. King,<sup>3</sup> Archibald,<sup>4</sup> and Reynolds<sup>5</sup> reported against Campbell's process; A. B. Taylor<sup>6</sup> showed that the idea of long maceration is a good one. Campbell apparently abandoned the process later.<sup>7</sup>

Calvert<sup>8</sup> suggested an apparatus for percolating with very volatile solvents which consists of two "aspirator" bottles one of which is set on a shelf and used as a reservoir for menstruum while the other is inverted and serves as the percolator. The two bottles are connected by tubing between the lower apertures. Menstruum flows from the reservoir into the percolator and the percolate may be collected out of contact with the air.

Taylor has suggested<sup>9</sup> using a portion of the finished preparation from a previous batch to moisten the drug and to start percolation before adding the menstruum. Dieterich<sup>10</sup> describes the Christ-Dieterich percolator the essential feature of which is an inverted bottle of menstruum set into the top of the apparatus to furnish an automatic supply of menstruum.

Army<sup>11</sup> has devoted much attention to the study of loss of vola-

<sup>1</sup> This Journal, Vol. 41, 384, (1869).

<sup>2</sup> This Journal, Vol. 41, 384, (1869).

<sup>3</sup> This Journal, Vol. 42, 29, (1870).

<sup>4</sup> This Journal, Vol. 42, 117, (1870).

<sup>5</sup> This Journal, Vol. 41, 525, (1869).

<sup>6</sup> *Proc. A. Ph. A.* 1869, 390.

<sup>7</sup> This Journal, Vol. 44, 102, (1872).

<sup>8</sup> This Journal, Vol. 55, 269, (1883).

<sup>9</sup> This Journal, Vol. 55, 556, (1883).

<sup>10</sup> *Pharm. Centr.* 29, 168, (1888).

<sup>11</sup> *Proc. A. Ph. A.* 40, 169, (1892).

tile menstrua in percolation and has described three forms of apparatus designed to minimize this defect. In 1895 Forrest<sup>1</sup> described an apparatus for continuous percolation which consists of a series of percolators arranged so that the percolate from one becomes the menstruum for the next and so percolates through the series. A form of percolator for volatile menstrua was designed by Barnard.<sup>2</sup> The whole apparatus is air tight in this type and a small tube which extends from the receiver up through the drug in the percolator to the inside of the cover serves to convey the air displaced in the receiver to the top of the percolator. Wood<sup>3</sup> suggests a modification of the siphon delivery tube in the well-tube percolator. He arranges a pair of corks in the end of the tube in such a way that the percolate must drop slowly and its flow can be controlled. Phillips<sup>4</sup> described a very simple apparatus for hot percolation.

Barksdale<sup>5</sup> suggested a percolator fitted with a stirring device and operated as follows: the drug is placed in the percolator and a volume of menstruum equal to half the quantity of fluidextract which the drug should yield is poured on the drug. The whole is stirred for at least thirty minutes, allowed to macerate two days, and then the same volume of menstruum is added and percolation started. When the liquid has percolated through enough more menstruum is added to furnish a 75 per cent. reserve (by volume) and then the drug is exhausted by simple percolation and the weak percolate handled according to the official process. It is claimed that the drug is more quickly exhausted by this process than by the official one.

The "double-tube" percolator is an ingenious modification of Squibb's well-tube idea. An ordinary percolator is fitted with a central tube of rather large bore around which the drug is packed in such a way that the percolate flows into the tube. Within this central tube is a smaller tube which extends through the spout of the percolator and is held in place by a cork or rubber nipple.

This inner tube may be raised or lowered to control the height of the menstruum in the drug, the rate of flow and the period of

<sup>1</sup> *Pharm. Jour.* 55, 538, (1895).

<sup>2</sup> Merck's Report, 1899, 220.

<sup>3</sup> *Pharm. Era*, 1899, 359.

<sup>4</sup> *West Drug*, 11, 210, (1889); from the *Pharm. Record*.

<sup>5</sup> *Ibid.* 21, 116, (1899).

<sup>6</sup> Remington, "Practice of Pharmacy," Ed. 5, 1907, 265.

maceration. This is a very convenient form of percolator and is worthy of extended trial. In the writer's experience it has proved well adapted for percolation and especially for interrupted processes. With this apparatus it is impossible to leave the drug accidentally without maceration as the level of the percolate is always as high as the inner tube.

Lloyd's still<sup>1</sup> is an apparatus designed for the extraction of drugs and the concentration of the percolate without the risk of alteration due to heat. The apparatus is complex and the reader must be referred to the treatise issued by Lloyd Bros. for an extended description of it.

A simpler form of apparatus for the preparation of extracts under reduced pressure was suggested by Beard<sup>2</sup> who uses a percolator fitted with a side tube like the larger tube of a Soxhlet extractor and conducts the percolation in a partial vacuum.

#### PERCOLATION *versus* MACERATION.

Maceration as a process for the extraction of drugs has ever been a rival of the more popular process which supplanted it in 1833. From time to time advocates of maceration rise and attempt to do away with percolation as the official process. Weber,<sup>3</sup> Schmitt,<sup>4</sup> and a writer in the *Répertoire de Pharmacie*<sup>5</sup> have marshalled arguments in favor of the older method. Edel<sup>6</sup> has answered some of these.

It is claimed that the products made by maceration are more uniform and produce less precipitation than those made by percolation, that the process is very much simpler and not so liable to accident in inexpert hands, and that it takes less time.

The advocates of maceration forget that the process of percolation was designed originally to remedy a serious defect in the earlier procedure, namely the fact that a certain proportion of the extract was always retained in the drug and that, therefore, the liquid extract obtained by maceration did not represent 100 per cent. of the drug but only a fraction of that figure. Remaceration,

<sup>1</sup> U. S. Patent No. 777,115. The treatise is known as "The Development of the Pharmaceutical Still," 1905.

<sup>2</sup> *Jour. Am. Pharm. Assn.* 7, 964, (1918).

<sup>3</sup> *Drug. Circ.* 1898, 216; *Proc. A. Ph. A.* 1899, 381.

<sup>4</sup> *Pharm. Ztg.* 49, 102, 291, (1904); *Proc. A. Ph. A.* 1904, 283.

<sup>5</sup> *Proc. A. Ph. A.* 1882, 31.

<sup>6</sup> *West. Drug.* 1899, 57.

to be sure, would recover a large part of this retained extract but this would involve other difficulties which would rob the method of all advantages.

It is admitted that many tinctures may successfully be prepared by maceration and that maceration is more practicable for tinctures of certain resinous drugs than percolation, but for concentrated preparations like fluidextracts where the exhaustion of the drug is to be accomplished with as little menstruum as possible maceration is distinctly a failure. This seems to be the concensus of opinion among American pharmacists.<sup>1</sup>

The following figures<sup>2</sup> show plainly that maceration does not equal simple percolation. 750 Gms. of gentian root were treated with 1950 Gms. of dilute alcohol. One such batch was macerated for four days and pressed out; another was percolated.

	Percolated.	Macerated.
Volume of product,	1005 Mils.	1530 Mils.
Specific gravity,	0.958	0.931
Dry extract,	185 Gms.	174 Gms.
Gm. extract per 100 Mils. <sup>3</sup>	18.40 Gms.	11.37 Gms.

That tinctures made by maceration precipitate less than those made by percolation is hardly true for the majority of causes for precipitation exist equally in both cases. With fluidextracts where factors which induce precipitation are introduced by the evaporation of weak percolate we should expect more of this feature. It is true, however, that in maceration the bulk of the precipitation takes place in the macerating vessel and, therefore, is not as apparent as it is in percolation but it is, nevertheless, as real.

Percolation is unquestionably a more complicated and difficult process than maceration and demands more knowledge of the art of pharmacy from the operator but this cannot be considered a valid argument against the process. We have a right to demand that a pharmacist be familiar with and expert in the processes of his art. Consequently any sacrifice of product quality for the sake of simplifying a method is unjustifiable. The experience of a century has led to the retaining of the process of simple percolation as the best general method for the extraction of drugs.

<sup>1</sup> This Journal, Vol. 61, 187, (1909).

<sup>2</sup> Herzog, *Ber. d. d. Pharm. Ges.* 15, 107, (1905).

<sup>3</sup> These figures added by the writer.

#### THE PRODUCT.

The product of the process of percolation is the percolate. If this is subjected to any further treatment, with the possible exception of filtration, some other distinct process is involved. The percolate is not, however, in condition for use except in the preparation of tinctures, wines, certain elixirs, or if repercolation has been employed and, consequently, is frequently processed again. Much study has been made of the percolate and the various methods of treatment applied to it and, while this aspect of the subject is strictly outside the limits of percolation, the further treatment of percolates is so intimately connected with the extraction process that no account of the latter would be complete without a consideration of the fate of the product.

In the manufacture of solid extracts the whole of the percolate is evaporated nearly to dryness; for fluid extracts this evaporation is confined to the "weak" percolate which is concentrated only as far as the volume of the reserved portion necessitates. During the evaporation of an alcoholic percolate practically all of the alcohol vaporizes early leaving the extractive in contact with hot water.

The temperature at which the evaporation is conducted may affect the quality of the ultimate product especially in such cases where easily decomposed or rearranged substances are present and particularly in acid liquids. In the latter case it must be remembered that evaporation increases the concentration of the acid and even if it is a weak acid it may become concentrated enough to hydrolyze glucosides and decompose alkaloids.

It is, therefore, advisable to conduct all evaporations under reduced pressure but is not absolutely necessary to do so in every case. A certain amount of hydrolysis and decomposition will occur no matter how carefully an evaporation is conducted even *in vacuo*; indeed, hydrolysis will take place in tinctures of some drugs which have not been subjected to heat at any stage of their preparation.

The changes which take place in the extracted matter during evaporation have been studied but they are of so complicated a nature and involve so many substances about which we know little that our knowledge of this whole subject is only fragmentary. We have merely a superficial idea of the nature of substances as they exist in the living cell and can, therefore, state little about the changes which they undergo in reaching a form in which we may investigate them. I think that much time and energy have been

devoted by pharmacists to a prevention of changes which are, for pharmaceutical purposes, often wholly unimportant. If proteins are coagulated, starch precipitated, carbohydrates caramelized, and non-medicinal tannins oxidized what does it matter? The essential purpose is the preservation of therapeutic value and if this is accomplished the important part of the process is successful.

And that precipitation, oxidation, and other phenomena to which evaporation is liable to lead are not usually fatal the following evidence is offered: Diehl<sup>1</sup> stated that the moderate heat required in the preparation of fluidextracts does not injure them. Maisch was of the same opinion and a fluidextract of Ipecac made by him about 1864 by an evaporation process was analyzed by Lawall in 1897<sup>2</sup> and found to be above U. S. P. strength even after thirty years.

An investigation of the nature of precipitates in tinctures was reported by Cripps<sup>3</sup> who found the following: the deposit in Tr. Calumba contained none of the active principles; that in Tr. Cardamom Comp. was almost wholly calcium tartrate; tinctures of cinchona (B. P.) exhibited precipitates which contained varying amounts of alkaloids in combination with tannoids; the deposit in Tr. Gentian Comp. was starch, gentian sugar, and albuminous matter, that in a concentrated Tr. Ipecac did not contain emetine; a deposit in a tincture of quinine was calcium sulphate; one in tincture of rhubarb contained gummy matters, calcium oxalate, with a little magnesium and chrysophanic acid. It may thus be seen that in a great number of cases a precipitate contains nothing of therapeutic importance. If an active ingredient separates the fault is with the solvent or the associated compounds.

#### PRECIPITATION IN FLUIDEXTRACTS.

This subject, because of its great importance, has received much attention from pharmacists. Maisch,<sup>4</sup> Lilly,<sup>5</sup> Diehl,<sup>6</sup> Lloyd,<sup>7</sup> and others have given careful consideration to the causes of precipitation.

<sup>1</sup> *Proc. A. Ph. A.* 1879, 727.

<sup>2</sup> This Journal, Vol. 69, 619, (1897).

<sup>3</sup> *Pharm. Jour. Trans.* 43, 483, (1883); This Journal, Vol. 56, 101, (1884).

<sup>4</sup> This Journal, Vol. 31, 113, (1859).

<sup>5</sup> *Pharm. Rec.* 1888, 233.

<sup>6</sup> *Proc. A. Ph. A.* 1878, 681.

<sup>7</sup> *Proc. A. Ph. A.* Vol. 1881, 408, 421; 1882, 508; 1883, 336; 1884, 410; 1885, 411; This Journal, Vol. 56, 499, (1884).

Lloyd has said, "I must say that it does not seem probable that we shall ever, by percolation alone, succeed in making a line of permanent fluidextracts from dry plants. The most important of steps then, is to adapt our menstruum so that it may hold in solution the medicinal principles of each plant and thus render the precipitate which forms inert; for the precipitate will follow."

The known causes of precipitation are: variation in the composition of menstrua whereby extracted matter obtained under different conditions is introduced into a preparation; introduction of water by evaporation of weak percolates and addition to the reserve; oxidation of soluble substances with the production of



PROF. JOHN URI LLOYD

Inventor of the Lloyd extraction apparatus; author of valuable papers on the precipitates in fluidextracts.

insoluble matters: changes of temperature; chemical changes within the solution; the presence of inorganic matters; the presence of minute particles of insoluble substances which at first are invisible but later agglomerate and cause a deposit. It has been shown that light does not cause precipitation.

An interesting effect of precipitation was observed by Lloyd.<sup>1</sup> He found that there is considerable difference between the alcoholic content of a freshly prepared fluidextract and the same preparation after it has precipitated. In the case of *Fldext. Podophyllum* the change was from 53 per cent. to 65 per cent., in *Jalap*, 83 per cent.

<sup>1</sup> *Eclectic Med. Gleaner*, 3, 505, (1897); This Journal, Vol. 80, 39, (1908).

to 98 per cent., Eriodictyon from 77 per cent. to 86 per cent., Grindelia, 83 per cent. to 90 per cent. so that a fluidextract which has precipitated will show, on analysis, a larger percentage of alcohol than is declared on the label.

#### CONCLUSION.

We have now considered every phase of the process of percolation beginning with the apparatus and continuing with a discussion of the drug and its preparation for percolation and an analysis of the mechanism of extraction to an account of the various improved methods and apparatus suggested during the past hundred years.

Some new ideas and certain novel ways of regarding different aspects of the subject have been presented and a portion of these, at least, are at variance with current notions.

The whole survey emphasizes the need for more investigations of the process of percolation and particularly investigations in which the time-factor is not ignored. It is recommended that Colleges of Pharmacy might well include some of this work in their courses on the practise of pharmacy especially with advanced students, many of whom would welcome an opportunity to contribute to our knowledge. In addition to its considerable educational value, such an arrangement would furnish us with a great mass of data our supply of which is to-day very meager.

One of the chief reasons for writing this paper has been a desire to direct attention to and stimulate investigation of the many problems of percolation which still await solution.

#### SUMMARY.

A general survey of all our published knowledge on the subject of percolation has been made. This knowledge has been classified, coördinated, and subjected to critical analysis. The results of every important contribution are presented and the best technique under varying conditions, as determined by the experience of the whole body of pharmacists, stated.

Certain factors which bear on the problems of percolation and have not yet been investigated are discussed and attention is directed to other factors which require reinvestigation owing to the inadequateness of our present data.

Explanations for a number of phenomena observed during percolation are offered and a discussion of the mechanism of extraction is included.



A section of this survey deals with the various processes and forms of apparatus designed to solve some of the problems of simple percolation, especially such methods as repercolation and interrupted percolation.

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## REVIEW OF TESTS FOR METHYL SALICYLATE IN OILS OF GAULTHERIA AND BIRCH.\*

BY CHARLES H. LAWALL, PH.M.,  
PHILADELPHIA, PA.

Periodicity is one of the commonest of natural phenomena. Man having caught the spirit of nature follows close after in this respect, hence the common adage about history repeating itself. This is particularly true of certain lines of scientific investigation. A particular instance is that of the tests for distinguishing between oil of gaultheria, oil of birch and methyl salicylate, and of detecting mixtures of these oils, for which a new method is published every few years. The reason for this search is found in the wide difference in price and the temptation to mix them or substitute one for the other.

There are certain fundamental factors in a problem of this kind which point to the probability of a test being devised for distinguishing the pure oils, but an equal improbability of any infallible method being discovered of detecting admixtures of one with the other, even in large amounts. In support of this belief let me state my reasons:

Without going fully into the chemistry of the respective oils, it will suffice to say that the differences between them are essentially as follows:

(1) Methyl salicylate is a distinct chemical entity and appears upon the market as such in a state of high purity.

(2) Oil of gaultheria consists of methyl salicylate to the extent of 99 per cent., the balance consisting of a paraffin, an aldehyde, a ketone, an alcohol and an ester.

(3) Oil of birch consists of methyl salicylate to the extent of over 99.5 per cent., the remaining trace consisting of the paraffin and ester, but not the alcohol nor aldehyde.

\* Read at the October meeting of the Philadelphia Branch of the A. Ph. A.

It is certain in the light of the foregoing premises that any distinguishing tests must be based upon differences due to the traces of associated substances in birch and gaultheria oils, respectively, for the methyl salicylate factor is common to all three products.

It likewise follows that there is absolutely no hope of any test for detecting added methyl salicylate in either oil of birch or oil of gaultheria by a positive reaction if the methyl salicylate be pure for pure methyl salicylate reacts similarly whatever its origin.

Any possibility of distinguishing these oils, therefore, must be based upon the discovery of a test which will identify these elusive factors which are present in scarcely more than traces in oils of birch and gaultheria, respectively, and to detect mixtures it would be necessary to discover a method which can be transformed into a quantitative reaction or one in which advantage can be taken of its intensity.

The only reactions of a distinguishing nature likely to be discovered are color reactions, and as color reactions are usually uncertain and when translated into colorimetric methods for quantitative use, are rarely very accurate, the chances of accomplishing anything of real value in this research are seen to be very remote, for it is only of academic importance to be able to distinguish the products in a state of purity if mixtures of one with the other cannot be detected with certainty.

From time to time investigators have pursued this *ignis fatuus* of a color reaction which should serve both as a distinguishing test of the pure substances and a method of detecting admixtures, completely ignoring the fallacy of such a quest.

In 1913, Stanislaus and Semmel, in the *Proceedings of the Pennsylvania Pharmaceutical Association*, proposed several reagents for accomplishing this result. The reagents consisted of nitric acid, sulphuric acid and formaldehyde mixed in several combinations. The resulting color reactions with the three products were described as brown, light brown and yellow; straw, light straw and light yellow; amber, yellow and colorless. There is not enough distinctiveness about tests giving such results to make them worthy of consideration as affording hope of detecting mixtures.

In 1914, Watson and Sayre, in the *J. A. Ph. A.*, p. 1658-9, proposed several tests. One was based upon differences of color produced in the three products by sulphuric acid. The reactions are described as dark red, yellow or light red, and colorless for oils

of gaultheria and birch and methyl salicylate, respectively. Assuming that the pure products give these reactions, the chances of detecting methyl salicylate in either of the natural oils would be very slight even if large amounts were added. Another reaction proposed by these authors is based upon colors produced by a mixture of sulphuric acid and an alcoholic solution of heliotropin. The reactions produced in gaultheria, birch and methyl salicylate, respectively, are crimson, less intense crimson and yellow. It is obvious that the same criticism applies here as to the previously mentioned test with regards to the possibility of its being applied quantitatively even in an approximate manner. Still another test proposed by these same authors is applied by adding, successively, sulphuric acid and a saturated aqueous solution of chloral hydrate. With this test the color reactions are more distinctive. The gaultheria gives a green color, the birch a violet, while methyl salicylate gives no color.

I have found this test to give very satisfactory results when some pure samples of the respective products are used, but with mixtures there is no quantitative distinctiveness about the test, the shades of color being influenced more by slight variations in the proportions of the reagents than by differences in the amounts of the respective oils, and the hope that the authors express, that the test may be made quantitative, has not been substantiated by any subsequent work done by the authors of the test themselves or by any other worker who has published his results, although four years have passed since the test was first published.

In 1914, F. C. Umney (*Perfumery and Essential Oil Record*, p. 60) published a test which has been widely quoted and frequently used, as follows:

"To five drops of the oil in a test-tube add five drops of a five per cent. alcoholic solution of vanillin and 1 Cc. of alcohol. Shake well and add 2 Cc. of concentrated sulphuric acid and mix thoroughly." Oil of gaultheria by this test is reported to give an intense crimson color; oil of birch a reddish brown and methyl salicylate a yellow color.

This test is subject to the same defects as some of those previously criticised, in that the methyl salicylate reacts negatively and very large amounts must be added before one can state with certainty that the sample is not pure. It certainly does give a distinctive reaction with some specimens of gaultheria oil.

It is not a difficult matter to devise new tests which appear to give distinctive results working with a single set of authentic samples. I have discovered several such tests in the short time with which I worked in the preparation of this article. It occurred to me that inasmuch as both gaultheria and birch oils are made from drugs which contain more or less woody cellular tissue, that conditions would be favorable for the production of furfuraldehyde in the distillation of these oils, and it will be noted that an aldehyde has been reported in gaultheria oil, although its identity was not established. The application of several of the better known tests for furfuraldehyde, notably the aniline acetate test, such as is used for detecting invert sugar in honey, were applied and, as was expected, positive results were obtained. With this test, for instance, a specimen of authentic gaultheria oil gave an immediate intense red color; birch oil gave a pronounced red color, more slow in its appearance, and methyl salicylate gave a negligible reaction. Other tests for furfuraldehyde, as, for example, the Badouin test for sesame oil, in which hydrochloric acid containing one per cent. of sugar is the reagent, also showed differences in the intensity of the reaction, but when applied to mixtures the test becomes practically valueless, for reasons explained in connection with several of the foregoing tests. It would be easy, also, to defeat the objects of such a test by the addition of a small amount of furfuraldehyde to the methyl salicylate used for adulteration purposes.

At times during the past five or six years it has been stated in print (Schimmel's Report, April, 1914, p. 99) or the rumor has circulated throughout the essential oil trade that the U. S. Department of Agriculture chemists are in possession of a test which enables the detection of adulteration of gaultheria or birch oils with methyl salicylate with certainty. Such test has never been published and if it exists it is probably based upon one of the previously published tests or upon some such reaction as the one I have described for furfuraldehyde, for instances might be found of adulteration so gross, say 90 per cent. of methyl salicylate to 10 per cent. of the genuine oil, that a difference in intensity could be noted. It is more likely that the majority of the prosecutions which have been brought for adulterations of this kind have been based upon inspectors' actual knowledge of admixture.

I have at various times been presented with so-called authentic samples of oils of gaultheria and oil of birch. Three of these sam-

ples possess the negative optical rotation required of gaultheria oil by the U. S. Pharmacopœia. Applying all of the color reactions so far described in the literature of these oils the variations in effect are so marked as to impel the conclusion that there is not likely to be a test which will give uniform results with all authentic samples.

Only one of the three laevorotatory oils gives positive results with Sayre and Watson's chloral hydrate test, and this same sample is the only one which gives positive results with Umney's test. If one relied upon the U. S. P. tests alone they would all pass. Are we to infer that the laevorotatory power is not distinctive of gaultheria oil?

I believe the answer to this question and the explanation of all other inconsistencies in these color reactions is that they are only satisfactory with some samples distilled under certain conditions, and that no test has ever been subjected to the searching application of many authentic samples.

Inasmuch as clinical experiments on the part of investigators working on behalf of the American Medical Association have declared that the natural salicylates have no therapeutic advantage over the synthetic salicylates of equal purity and not one observer in ten can distinguish between unlabeled samples of oils of gaultheria birch and methyl salicylate as regards odor, the final conclusion is: What's the Use? Let's work on something worth while.

DEPARTMENT OF PHARMACY,  
PHILA. COLLEGE OF PHARMACY AND SCIENCE.

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## THE PHARMACEUTICAL PLANT CHEMICAL SOCIETY.

BY GEO. E. ÉWE,

PHILADELPHIA, PA.

A Chemical Society organized among the employees of a plant yields the same primary benefits which surround membership in a nationally organized Chemical Society. Among these benefits may be mentioned, mutual exchange of valuable information; mutual sympathy and assistance in the solving of difficult chemical problems; coördinated effort on chemical matters in general, and social features.

The Plant Chemical Society, however, yields additional benefits:

It acquaints each member with the character of the work being performed by each of the other members, thus leading to teamwork.

It affords a forum for the open and unbiased discussion of technical misunderstandings which are hindering the progress of the work of the plant.

It affords an opportunity to the management of announcing and explaining innovations, thus securing the coöperation of the members and eliminating the normal antagonism to innovations put into operation without explanation.

It affords to both the management and employees the opportunity of presenting and discussing new policies which will advance the work and the prestige of the plant, or discussing existing policies which are hindering the work or damaging the prestige of the plant.

It affords the opportunity of issuing and explaining general instructions on a wholesale plan, thus conserving the time ordinarily expended by the individual discussions and explanations by letter or conference which usually follow the issuance of general instructions on an individual plan.

It affords an opportunity to the member to present his opinions regarding faults in products and processes and to present suggestions for the elimination or correction of the faults.

It affords an opportunity for the members to become better acquainted with each other socially, with the result that mutual sympathy and regard is engendered.

The final and desired result of the Plant Chemical Society is to increase the interest of the member in the scientific aspect of the work of the plant. The importance of this result is attested by the fact that only an interested employee is satisfactory to the highest degree.

In April, 1914, a Chemical Society was established in the plant with which I am connected and the success of the movement has been so thoroughly proven, that I feel warranted in offering an explanation regarding the methods employed in the establishment and conductance of the Society, for the guidance of those plants in which no similar organization is conducted at present.

The plans upon which the Society was organized and is being conducted are, no doubt, capable of improvement, but, nevertheless, have yielded eminently satisfactory results.



The general statement of the aims and purposes of the Society which was presented for the consideration of the Charter Members at the initial meeting read as follows:

AIMS AND PURPOSES OF THE . . . . . CHEMICAL SOCIETY.

Benefit to the members by reason of knowledge imparted and ability increased through the activities of the Society; especially regarding chemical and analytical chemical matters.

To give to the members, in some degree, a post-graduate course in the chemistry pertaining to the plant.

To give to the members practice in the accurate reporting of results of chemical work.

To increase active interest in the scientific aspect of the work being performed by the . . . . . Co.

To acquaint each member with the work being performed by each other member.

To invite discussion of ways and means of best performing the chemical work of the plant.

To propagate mutual assistance in solving difficult chemical problems.

To discuss any matter which may prove of value to the members of the Society, if considered worth while by the Chairman of the Society.

This statement of aims and purposes was unanimously adopted and has operated satisfactorily to this date, without amendment.

The rules for eligibility to membership are very broad and read as follows:

RULES FOR ELIGIBILITY TO MEMBERSHIP.

Any employee, preferably possessing chemical training and experience who can contribute to the benefit of the members, or who can be benefitted by becoming a member of the Society, may be a member.

A striking feature of the membership of this Society has been the number of nationalities represented. At various times, the Society has had the honor of having members originally emanating from Italy, China, Russia, Japan, Denmark, France, Holland, Roumania, Cuba, Austria and Germany. Thus the benefit of very many different viewpoints has been obtained upon the subjects under discussion.

## MEETINGS OF THE SOCIETY.

The meetings of the Society are held in the Research Department between four and five P.M. on any Friday, except holidays, whenever sufficient matters are in the hands of the Chairman to warrant a meeting. These meetings are called by the Chairman.

The Company, with which I am connected, has recognized the mutual advantages to be derived from membership in the Society and has granted permission for attendance at meetings held during working hours.

## OFFICERS OF THE SOCIETY.

At present only two officers are required, namely a Chairman and a Secretary. The Chairman is chosen by nomination and election at a regular meeting and then appoints the Secretary. The Chairman and Secretary hold office for three calendar months.

As a rule, the Secretary is nominated and elected as Chairman to succeed his retiring Chairman. The present arbitrary plan of choosing a Chairman and Secretary is based upon length of service with the Company, so that each member has the privilege of becoming Secretary and then Chairman in turn. This plan is not absolutely rigid, as reservation is held that appointment of an undesirable Secretary is not obligatory. However, to date, this plan has been followed without a break and with undoubted satisfaction.

The duties of the Chairman consist of collecting material for meetings, calling meetings, presiding at meetings, and appointing his Secretary.

The duties of the Secretary are to assist the Chairman in every possible way, take up the duties of the Chairman, when the Chairman is unable to functionate, record minutes of each meeting and read at each meeting the minutes of the preceding meeting.

## QUORUM NECESSARY FOR HOLDING MEETING.

The quorum necessary for holding a meeting was adopted as being one more than half the membership.

It might be well to note here that at no time, has it been impossible to obtain a quorum, when a meeting was called. No intimation of coercion is exercised to secure attendance at the meetings. The members appreciate the advantages to be derived from attendance. Every effort is made to make the meetings interesting and in order to accomplish this purpose, the practical, rather than the theoretical,

side of subjects is given preference, as it has been found to yield the best results. However, the theoretical side has not been neglected. Only a very few members have shown a lack of interest, chiefly due to inappreciation of the advantages to be gained from the subject matters of the meetings.

#### RELATION OF SOCIETY TO NON-MEMBERS.

On 5/22/14 it was unanimously decided that contributed papers and other information, when suitable, be presented to other chemical and pharmaceutical societies. Also, when the papers, etc., concern employees of the Company, who are non-members, that the papers, etc., be brought to the attention of these employees.

#### ORDER OF BUSINESS OF MEETINGS.

The order of business of meetings has gone through a series of changes, designed to accommodate it to the present needs of the Society and at present has the following form:

Call to order.

Reading of minutes of preceding meeting.

Old business.

Reading of contributed papers and notes.

New business.

Installation of new members.

Reading and disposal of correspondence.

Committee reports.

Announcement and discussion of changes and proposed changes in products and processes.

Announcement and discussion of new products and processes.

Miscellaneous announcements.

Reporting and discussion of items of daily work which are of general interest.

Election of officers (when in order).

Announcement of nature of chief business of next meeting.

Adjournment.

A brief discussion of some of the items of the order of business may prove of interest in indicating the purpose and value of these items.

The contribution of papers and notes to these meetings induces to a more thorough performance of certain tasks included in the daily work upon which these papers and notes are based. The member is encouraged to so perfect and round out his work that a

conclusive, interesting and readable report results. In some cases, special arrangements are made to assist the members in doing this. These arrangements include the providing of special materials, books and apparatus and the granting of freedom from usual tasks in order to provide the time for the work. This item of "order of business" has developed into one of the most successful activities of the Society. The papers and notes presented at the meetings total over two hundred for the six years of the existence of the Society. Most of these papers and notes consisted of proved suggestions for economy in labor and materials, the prevention and utilization of wastes and improvements in the products manufactured by and processes used in, the several Departments of the Company represented in the membership of the Society. Some of these papers were publishable and were published and others which carried suggestions which were of value to Departments of the Company which were not represented in the Society were presented to the consideration of these Departments accordingly.

The following list of titles of a few of the papers and notes presented at these meetings will indicate both the scientific and practical interest shown by the members of the Society in the business of the Company:

"The Assay of Tablets Containing Calomel and Calomel and Sodium Bicarbonate."

"Soft Gambir."

"Some Criticisms of (a Product Marketed by the Company)."

"The Determination of Potassium in Colloidal Silver Preparations."

"Standard for Dried and Powdered Magnesium Sulphate for Use in . . . . ."

"The inconsistency of designating (a Product Marketed by the Company) as an Elixir."

"The Taking of Samples for the Chemical Laboratory."

"Improvements in the Manufacture of Emetine Bismuth Iodide."

"The Assay of Creosote Tablets."

"The Duties of an Analytical Chemical Laboratory Connected with a Pharmaceutical Manufacturing Plant."

"The Time Required by Rennin for Coagulation of Milk is Inversely Proportional to the Amount of Rennin Employed."

"Uses of Centrifuges in the Analytical and Chemical Laboratories."



ings, some information of general interest he has gained. The Chairman of the meeting develops the importance of this item by editing the daily reports of each member before the date set for a meeting and suggesting to the member the submission of the interesting items in his reports. This item also affords the opportunity to each member to present his technical difficulties and obtain the opinions and help of the other members of the Society in solving the difficulties.

The item of "announcement of chief business of next meeting" affords the members the opportunity of announcing the titles of papers which they intend to present at the next meeting. Subjects for discussion or explanation may also be announced.

As evidence of the true scientific and practical interest developed by the Society, a copy of the minutes for the meeting held on 11/31/17 is herewith reproduced:

MINUTES OF THE 11/31/17 MEETING OF THE ..... CO.  
CHEMICAL SOCIETY.

Meeting called to order at 4.05 P.M.

Minutes of preceding meeting were read in abstract and approved.  
Old business: None.

Reading of contributed papers and notes: Note: "The Instability of (a Certain Commercial Preparation)." Paper: "The Emulsification of Liquid Petrolatum by Lanoline." Paper: "Emulsions of Liquid Petrolatum."

New business: Meeting room arrangements discussed.

Installation of new members: None.

Reading and disposal of correspondence: Several letters were read.

Committee reports: No committees out at present.

Announcement and discussion of changes and proposed changes in products and processes: The transfer of (a product marketed by the Company) to the list of products made extemporaneously upon order. Specific analytical chemical tests adopted for the selection of Glycerin for (a product marketed by the Company). Improvement in methods of manufacture and analysis for mercury in (a product marketed by the Company).

Announcement and discussion of new products and processes: The addition of (a product marketed by the Company) to our list

of products was announced; its method of manufacture and standardization was discussed.

Miscellaneous announcements: Several inter-departmental instructions. Meetings of the American Chemical Society, the American Pharmaceutical Association and Franklin Institute were announced; and also subjects to be considered at the meetings. The acquisition of several scientific books was announced.

Reporting and discussion of items of daily work of general interest: A large number of such items were reported and discussed. Among the items might be mentioned: "The application of emulsions of liquid petrolatum to the production of lipovaccines;" "The absence of Oil of Savin from the market;" "The size of samples submitted to the Analytical Department;" "Kieselguhr and Fuller's Earth as adsorbents of alkaloids;" "Some criticisms of U. S. P. tests;" "Conservation in the use of crucibles;" "Results of experiments on optimum temperature of drying (a product marketed by the Company) in order to hasten its manufacture;" "Traces of lead in zinc oxide and their effect on the human economy;" "A white product can be obtained by recrystallizing (a product marketed by the Company) from alcohol;" "Results of experiments to hasten drying of (a product marketed by the Company) by substituting other diluents for that now employed;" "The preparation and uses of Ammonium-Ricinol-Sulphonate;" "The deterioration noted upon compression of rennin tablets and measures required for the manufacture of standardized rennin tablets."

Election of officers: Not in order.

Announcement of chief business of next meeting: Papers on "The Manufacture and Pharmaceutical Uses of Cephaeline," and "The Determination of Chloral Hydrate in (a Product Marketed by the Company)," were announced. The subject of "Methods of Hastening the Washing of (a Product Marketed by the Company)" was announced for discussion.

Adjournment: Meeting adjourned at 5.05 P.M.

Conclusions: The aims and purposes of this Society have been amply fulfilled; the members have received the combined experience of the entire membership; the interest of the members has been enlisted in the solution of difficult technical and scientific problems; the members have received instruction in many subjects, allied to the work, with which they would not otherwise have come into contact; the quality of the chemical work of members has been im-

proved; products and processes have been elaborated and improved; practice in the accurate reporting of results of chemical work has been attained by the members; mutual understanding has resulted from the personal contact and discussion at the meetings, and "esprit-de-corps" has been furthered.

The chief purpose of this communication is to bring to the attention of Pharmaceutical plant operators the idea of conducting a Chemical Society in connection with the plant and to point out the benefits to be derived therefrom.

The general plan of the establishment, aims and purposes and conductance of a Pharmaceutical Chemical Society, as outlined above, is entirely amenable to improvement and further development. It is not offered as rigid and unalterable but can be rearranged, abstracted from or added to to meet the demands or desires of any particular plant.

PHARMACEUTICAL RESEARCH LABORATORY,  
H. K. MULFORD COMPANY,  
PHILADELPHIA, PA.

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## WOOD ALCOHOL NO LONGER: HEREAFTER METHANOL.\*

BY CHARLES BASKERVILLE,

COLLEGE OF THE CITY OF NEW YORK, NEW YORK, N. Y.

Wood (methyl) alcohol poisoning is an unique problem in that it involves not alone physiological changes and technical matters having to do with production and distribution of the toxic agent, but sociological factors as well.

The "adiophorous" spirit obtained by distilling wood (Boyle, 1661) was thought by Taylor (1812) to be a new kind of *ether*; in fact, he called it "pyroligneous aether." Dumas and Peligot (1835) established its resemblance to ethyl (*ether*) alcohol and named it methyl alcohol from the Greek μέθυ mead and ὕλη wood. In fact it may be recalled that the word *alcohol*, derived from the Arabic, *Al Kohl*, at one time meant a fine powder and only later meant spirits.

Commercially the destructive distillation of hard woods (refuse) is the main practical method followed for the production of methyl

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alcohol in America, although in Europe it has been obtained from peat and as a by-product from vinasse, and in the manufacture of wood pulp by a soluble sulfite process. The numerous synthetic methods known at present are too costly to be practiced on a commercial scale. The condensed tarry and acid products distilled from wood are subjected to partial purification by distillation. This crude material, about 80 per cent. pure, is then usually shipped to centrally located refineries in tank cars, drums, or barrels for further purification and rectification.

This crude wood alcohol, "wood spirit," "wood naphtha," a vile-smelling, greenish yellow to dark brown, nauseous liquid, is a complex mixture containing a variety of impurities. They are removed in the main in the first refining, yielding a product containing about 95 per cent. methyl hydroxide. In 1890 processes for greater refinement were put into operation, so that about 1906 a deodorized product (97 to nearly 100 per cent.) was placed upon the market in the United States under such names as "Columbian Spirits," "Eagle Spirits," "Hastings Spirits," "Colonial Spirits," "Manhattan Spirits," "Union Spirits," and "Lion d'or;" in Canada as "greenwood spirits," and "standard wood spirits;" and in Germany in 1912 as "pro spirit." Technically it was called methyl hydrate, carbinol, methylic alcohol, methyl hydroxide, and methanol. The pure substance is a colorless, mobile liquid, having a pure vinous odor, similar to that of pure ethyl alcohol, and possesses a burning taste.

These facts of names and their meanings are not known by all technical men. They are even less known to the "man-of-the-street;" but the layman does know that "alcohol" is the stuff which makes drunk come; that it is the stuff that cheers when down-hearted; that uncontrolled it has been a curse in the world; that it is the "real thing" in the disguise of beer or light wine, which formerly rested him when the arduous day's work was done. So when he sees the can or vessel with the label "alcohol" on it, and as he knows "alcohol" is the thing that gives the "kick," rest, or cheer, without considering the qualifying words "wood," "methyl," or what not, he is going to take it. He is little deterred by the "poison" label, for he has a more or less similar idea from the pictures of intemperance, and still he drank. Therefore, the term *alcohol* should cease its present significant use, at least in chemical literature. Technically, all alcohols should become known as "-ol" bodies or

hydroxides, as "methanol," "ethanol," "propanol," "butanol," etc.; methyl hydroxide, ethyl hydroxide, propyl hydroxides, etc.

In 1906 after a vigorous campaign the United States followed England, France, Germany, and other European countries by enacting laws permitting the general use of a tax-free domestic alcohol for industrial purposes, and for light, heat, and power.<sup>1</sup> This law has made us a self-contained nation in regard to certain medicinals; ether, ethyl chloride, chloral hydrate, nitrous ether, and numerous synthetics may be mentioned in illustration. To emasculate alcohol, as it were, the law requires that tax-free alcohol for use in the arts and industries shall have first mixed with it (under close supervision) substances which "destroy its character as a beverage or render it unfit for liquid medicinal purposes." On account of its poisonous properties, difficulty of removal from the resulting industrial alcohol, non-interference with many of the industrial purposes for which the denatured product was intended, and a desire to avoid the destruction of the methyl alcohol business, for methyl alcohol was cheap at that time, the first act designated it as a denaturant, and the Commissioner of Internal Revenue selected it as the principal one.

Up to date some forty-one formulas for "specially denatured alcohol," to be used for designated purposes only, have been authorized under the several acts. Five formulas for "completely denatured alcohol," which may be used for light, heat, and power, have been authorized. One of each of these has been revoked.

The control of the former class (special) is so complete, involving as it does the moral character of the users, that little danger attends its use. One formula (No. 30) allows the addition of as much as 10 per cent. of the purest methyl hydroxide, but its use is restricted to general chemical and physical laboratory purposes.

The latter class (completely denatured) promises some needed relief for the liquid fuel shortage and may consume much the largest portion of denatured alcohol. That means denatured alcohol will become even more common than it is now.

Data collected prior to 1918 indicated that the drinking of liquids containing methyl hydroxide was responsible for many deaths and acute cases of blindness.<sup>2</sup> The "deodorized" methanol

<sup>1</sup> Act of Congress, June 7, 1906; amended March 2, 1907; Act, October 3, 1913.

<sup>2</sup> See extensive report to the New York State Factory Investigating Commission, 1913, by the author.

resembles pure ethanol so closely that the ordinary layman can hardly distinguish the difference between the two. In complex mixtures, whisky, etc., its detection involves very careful chemical analysis. Formerly it cost less than ethanol, so unscrupulous people were tempted to use it as substitute for ethanol in adulterating whisky, essences, extracts, bitters, washes, liniments, balsams, perfumes, etc. The victims were generally those who indulged in the commoner forms of whisky, rum, and wine, although persons not addicted to the use of intoxicating drinks were undoubtedly often affected innocently from drinking Jamaica ginger, lemon extract, essences, bitters, medicines, etc., whose chief menstruum was "deodorized" wood alcohol. At one time the poorer negroes in the Southwest drank it under the name of "white horse" or "old mule." Happily, the abuses grew less through the operation of the National Pure Food and Drugs Act of June, 1906. However, during the penumbra of prohibition many cases of blindness and death occurred through the drinking of wood alcohol or denatured alcohol.

The "completely denatured alcohol" is the more readily obtainable. Formula No. 1 called for 10 per cent. of specified commercial methyl alcohol with one-half of 1 per cent. of approved benzine. This has been, and is, used in radiator water of motor vehicles to make a non-freezing mixture. This may account in part for the cases traced to garages. After the outbreak referred to, this formula was revoked December 29 last, appearing in orders issued January 8, 1920. Hereafter no completely denatured alcohol containing more than 2 per cent. methanol will be allowed. As alcohol of strengths above 80 per cent. require dilution before drinking, it is doubtful if any future acute cases may be attributed to denatured alcohol, that is, after the present outstanding stocks under Formula No. 1 are used up.

However, we cannot be so hopeful in regard to chronic cases culminating in blindness or defective vision which may be attributed to drinking diluted denatured alcohol containing methanol. The denaturing deterrents are selected primarily on account of the nauseous odor and repulsive taste, rather than physiological action. These odors and tastes repel some people. "Rot gut" whiskies and some "mountain dew" are not far behind varieties of denatured alcohol in odor and taste. With added flavoring, denatured alcohol containing 2 per cent. of methanol may be diluted until it contains 1 per cent. or less of methyl hydroxide, and be drunk. Death is

not to be expected, immediate nor early blindness, from such a draught. And therein lies the danger, so apparent to all who are familiar with the cumulative action of drugs and the insidious influence of liquor.

Proper doses of paraldehyde produce some physiological effects associated with ethyl alcohol. It has been stated, but not authoritatively supported, that paraldehyde was shipped to Russia from another country (not the United States) to serve as a substitute for vodka. We are familiar with the historic accounts of ether sprees indulged in by the Irish and "Piccadilly Willies," and recent medical literature tells of the successful use of oil-ether cocktails prior to dressings of seriously wounded soldiers. So a variety of intoxicants and exhilarating soporifics are actually available, but their names and associations are those of *drugs*, hence their use is not common. If we can but divorce the name and promote the recognition that these "-ol" bodies are in fact drugs and dangerous, liable to produce blindness, the very element of fear alone will have a most salutary effect in protecting men and women from themselves.

Producers of 90 per cent. of the refined methyl hydroxide in this country have decided that hereafter all packages containing it shall be labelled "methanol," and so their advertisements read in the trade journals this day.

This change in nomenclature has been recognized, but the usage cannot be brought about instantaneously and will require time. The word will continue as a synonym in any event, although through concerted action it may become more or less obsolete. No form of legislation can eliminate the name. This is an appeal to chemists to assist.

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## THE DETERMINATION OF HYDROCYANIC ACID.\*

BY R. LEITCH MORRIS, F.I.C.

For the determination of cyanides, a number of volumetric processes have been used.

The principal are:

1. The original process of Liebig: Titration of the alkaline cyanide solution with standard silver solution.

This is quite satisfactory when properly carried out.

\*Reprinted from *The Pharmaceutical Journal and Pharmacist*, July, 24, 1920.

2. Method of Fordos and Gelis: Little used, but useful in special cases, *e.g.*, for mercuric cyanide.

3. Volhard's method: Complete precipitation as silver cyanide by adding excess of standard silver solution, filtering, and then determining the excess of silver in the filtrate by standard thiocyanate.

4. Titration of cyanide by Mohr's method, using potassium chromate indicator of the complete precipitation.

5. Denigès' modification of Liebig's process, on which the process of the B. P. 1914 is based.

#### LIEBIG'S ORIGINAL PROCESS.

Properly applied, this method is quite satisfactory, but when free hydrocyanic acid is in question there are several possible sources of error.

The acid must be saturated with but a slight excess of NaOH to form the cyanide, and any *great* excess of NaOH delays the end-point, hence leading to somewhat higher results. But a *deficiency* of NaOH causes a much more serious error, the results being then too low, and the greater the deficiency of NaOH the lower are the results. Results may be obtained showing only a mere fraction of the true strength in such cases: a serious matter in the testing of such a poisonous medicinal agent as hydrocyanic acid.

In the older analytical textbooks the directions are given to make the solution of HCN strongly alkaline, but since NaCN and KCN are strongly alkaline to litmus, this is no safe guide. A strongly alkaline reaction to litmus paper is obtained when only 10 per cent. of the free acid present is saturated. In such cases the process of Liebig gives the end-point when the NaCN present is converted completely into AgCN, NaCN, and so determines at this point the NaCN present. If, now, the free HCN remaining in solution is saturated with NaOH, the titration can be continued. The extra silver now used is equivalent to the free hydrocyanic acid remaining unsaturated at the first addition of the soda. When a solution contains alkaline cyanide and also free HCN this last process of titration allows of the determination of both in the same lot of solution.

These points were communicated to the meeting of the B. P. C. in 1874 in an excellent paper by Siebold. He stated that, for every 10 Cc. of normal soda present in excess of that required to form NaCN, an additional 0.1 Cc. of *N*/10 AgNO<sub>3</sub> was required. The error is small in this case, and even if this excess has been used, the

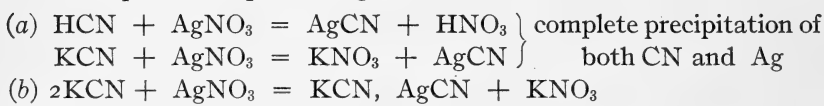
error on a 2 per cent. acid would only affect the percentage found, by a unit in the second decimal, if about 20 Cc. of  $N/10$   $\text{AgNO}_3$  were used. Evidently one is quite safe if the excess of soda is kept at about the equivalent of 1 or 2 Cc. of normal  $\text{NaOH}$ .

A study of the reactions involved explains the difference between Liebig's and the other processes in above list.

(a) When a solution of  $\text{HCN}$  or of an alkaline cyanide is added slowly to an excess of silver solution, precipitation of  $\text{AgCN}$  is immediate. The continued addition of  $\text{HCN}$  only increases the precipitate till all the silver is converted into  $\text{AgCN}$ . But continued addition of alkaline cyanide causes the precipitate first formed to redissolve as the double cyanide.

(b) Reversing the order of mixing:  $\text{AgNO}_3$  added slowly to an alkaline cyanide gives no permanent precipitate till all the cyanide is changed to the double salt, then the next drop of  $\text{AgNO}_3$  solution causes the beginning of precipitation of  $\text{AgCN}$  (the end-point in Liebig's process). The final *complete* precipitation of cyanide as  $\text{AgCN}$  is accomplished by adding exactly as much silver again as that used to cause the first sign of precipitation.

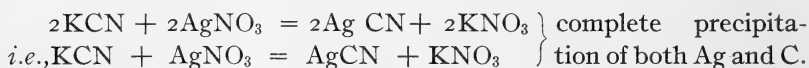
The equations representing *a* and *b* are:



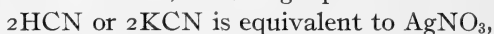
No precipitate till this stage (b) is complete. End-point of Liebig's process.

The addition of more  $\text{AgNO}_3$  precipitates  $\text{AgCN}$ .

Another molecule of  $\text{AgNO}_3$  gives the same final result as (a):



A point obvious from these equations which seems to have escaped notice is that since, in Liebig's process.



similarly  $2\text{KOH or } 2\text{NaOH}$  is equivalent to  $\text{AgNO}_3$ .

And therefore, the amount of alkali required for exact conversion of the  $\text{HCN}$  into cyanide is twice as many Cc. of  $N/10$   $\text{NaOH}$  (or  $\text{KOH}$ ) as the number of Cc. of silver solution used.

i.e., No. of Cc. of  $N/10$  silver required  $\times 2 =$  Cc. of  $N/10$  soda that should be used to convert the  $\text{HCN}$  into cyanide.

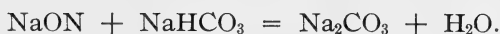
No. of Cc. of  $N/1$  silver  $\times 2 =$  Cc. of  $N/1$  soda required.

Taking 5 Cc. acid of 2 per cent. strength, which should require not more than 19 Cc.  $\text{AgNO}_3$ , the amount of  $N/10$  soda required would be 38 Cc. In this case the use of 4 Cc. of normal soda will ensure accurate results. Also, more than 10 Cc. of  $N/1$  soda should never be used, since this is sufficient for a titration in which 50 Cc. of  $N/10$   $\text{AgNO}_3$  are required.

From equations (a) and (b) it is obvious that in the case of HCN the addition of alkali is necessary to allow the Liebig reaction to take place by converting finally the  $\text{NHO}_3$  which would otherwise be liberated into  $\text{KNO}_3$ .

Evidently, for this purpose, alkaline carbonates would serve as well as hydroxides, and at first sight it would seem that this is an easy way of overcoming the difficulty by keeping the excess of alkali required sufficiently low. Were HCN not a volatile substance, such would be the case, but since HCN is a very weak acid, which barely reddens litmus, and *does not decompose carbonates*, it is obvious that, at the beginning of the titration, all the HCN present is in the free state, and some free HCN will be present up to the end, and this leads to loss owing to the continual agitation of the solution during titration.

After adding excess of alkaline hydroxide, however, this excess can be considerably reduced by the addition of a little sodium bicarbonate.



*Influence of Other Substances on Liebig's Process.*—Ammonium salts *would not interfere*, but free  $\text{NH}_3$  *does so*, as  $\text{AgCN}$  is soluble in ammonia, and if ammonium salts are present some free  $\text{NH}_3$  will be liberated by the excess of alkali. This can be overcome by addition of a little carbonic acid water; a bottle or syphon of aerated water is useful for the purpose. Addition of  $\text{NaHCO}_3$  is not suitable here.

Chlorides, bromides, and iodides do not interfere. Squire states in last two editions of the *Companion* that chlorides are also estimated in Liebig's original process, *but this is an error*.

If halogen salts are present the end-point (precipitation) is shown by the precipitation of the silver *halides*, which are *more* insoluble than  $\text{AgCN}$ , and this tends to make the end-point *sharper*. The average error in Liebig's process, should not exceed 2-3 parts per thousand too high. In Liebig's process 1 Cc.  $N/10$   $\text{AgNO}_3 = 0.005$ ,-404 Gm. HCN.

## 2. METHOD OF FORDOS AND GELIS.

This is also a very old process. The reaction was discovered by Serullas and Wöhler.  $\text{HCN} + \text{I}_2 = \text{HI} + \text{ICN}$ . Hence  $\text{I}_2$  is equivalent to HCN (or KCN) and 1 Cc. of  $N/10$  iodine = 0.001351 Gm. HCN. *Starch must not be used* as indicator, as its presence leads to low results. The solution must be highly diluted. In the case of alkaline cyanides, the solution, containing about 0.05 Gm. of cyanide, is diluted to about 400 Cc., a little  $\text{CO}_2$  water added, and iodine solution run in till a faintly visible yellow appears in the solution. In the case of HCN, sufficient NaOH is added to convert the acid to cyanide, excess of carbonic acid water added to convert excess of NaOH into bicarbonate, and the solution titrated in the same way. The results are generally a little *lower* than those obtained by Liebig's process, but are fairly close to the truth, although a little excess of iodine is necessary at this high dilution to give the solution the faintest visible tint. The process is somewhat troublesome for hydrocyanic acid. It is a useful process for determining CN in  $\text{HgCN}$ .

## 3. VOLHARD'S METHOD.

Volhard's method is only useful in special cases. It is highly accurate, but the necessary filtration of the silver cyanide before the excess of silver can be determined makes the process tedious. All the halogen elements interfere. In this case, 1 Cc.  $N/10$   $\text{AgNO}_3$  = 0.002702 Gm. HCN.

## 4. MOHR'S METHOD.

This resembles the usual titration of chlorides, etc., by  $\text{AgNO}_3$  using  $\text{K}_2\text{CrO}_4$  as indicator. The solution must be neutral and in the case of HCN this is accomplished by using MgO. The reaction is different from Liebig's reaction, since the end-point shows the complete precipitation of cyanide; equation (a) above. 1 Cc.  $N/10$   $\text{AgNO}_3$  = 0.002702 HCN. The acid is added to excess of MgO which must be chloride free, and titrated with silver as usual, with continual stirring. Though at one time official in U. S. P., the process has no advantage over that of Liebig.

## 5. MODIFICATION OF LIEBIG'S METHOD. (DENIGÈS)

Denigès (*Journ. de Pharm.*) [5] (XXIX) suggests the use of KI as an indicator in solutions rendered strongly alkaline with soda or ammonia, and states that in this manner the end-point is sharply



and quickly determined. (See *Y. B. P.*, 1894.) This causes at the end-point the precipitation of  $\text{AgI}$ , which is the *most insoluble* of all silver salts, and thus gives the most accurate results in any modification of Liebig's method. Again, since  $\text{AgI}$ , unlike  $\text{AgCl}$  and  $\text{AgBr}$ , is highly insoluble in ammoniacal water, the substitution of ammonia for the soda required in Liebig's process becomes possible, and a considerable excess of ammonia does not interfere. The use of ammoniacal  $\text{KI}$  solution has long been employed as indicator in the cyanide titration of nickel. The process of the *B. P.*, 1914, is based on this method. I found it highly accurate ten years ago, but the "Conference Research List" says that it is unsatisfactory, and I have been led to look up the exact details given in the *B. P.* and to compare them with those I followed, and also with those given by the *U. S. P.* and the French Codex.

The compilers of the *B. P.*, 1914, have apparently copied from the *U. S. P.*, and have overlooked the fact that the *U. S. P.* solution of  $\text{KI}$  is a 20 per cent. one, while the *B. P.* solution is only 10 per cent., yet the amount to be used is 3 drops in each case. On further comparison of these processes it appears that at the *end* of the titration of the *U. S. P.* process the total volume of solution will be about 37 Cc., while at the end of the *B. P.* process the volume will be about 80 Cc. Hence, in the *B. P.* process the mass concentration of  $\text{KI}$  in the solution at the end-point is only about a *fourth* as strong as in the *U. S. P.* process. It would seem, therefore, that the *B. P.* prescribes too little  $\text{KI}$  for the process to give a sharp end-point. May not this be the reason that the *B. P.* process has been found unsatisfactory?

The French Codex orders 10 drops of solution of  $\text{KI}$  (20 per cent. wt. in wt.) to be used with 10 Gms. of acid and 15 Cc. of  $\text{NH}_3$  solution and dilution to 200 Cc. Here the mass concentration of  $\text{KI}$  in the final volume is practically three times that of the *B. P.* I used 0.1 to 0.2 Gm. of  $\text{KI}$  in working on this process.

Another suggestion to improve Liebig's process is due to Guerin in 1906, who recommended the use of a 3 per cent. solution of borax as the alkaline agent in place of  $\text{NaOH}$ . This is excellent. I found the amount of silver used in comparative titrations agreed exactly with that required by the original Liebig method when the excess of alkali was kept as low as possible in the latter method. Any excess of borax is immaterial. Guerin states that ammonium salts must be absent, but that this difficulty can be avoided by adding 10 Cc. of

saturated solution of boric acid to the liquid before titration. I have not verified this last statement.

#### EXPERIMENTAL.

The results given were obtained in 1909. This work was an extension of some work on cyanide solutions, in which the ammoniacal iodide process had given the best results as compared with other methods.

As a standard for comparison the HCN was determined gravimetrically by weighing as silver cyanide, and, as a check, igniting the silver cyanide to constant weight, and weighing again the residual metallic silver. To prevent loss by volatilization the acid was added to sufficient ammonia in a stoppered flask, after previously ascertaining the weight of flask +  $\text{NH}_3$  solution and the total weight again found. The mixture was transferred to a beaker, excess of silver nitrate solution added, and then the whole acidified slightly with dilute  $\text{HNO}_3$ .

The precipitate was collected on asbestos in a Gooch crucible, dried at  $100^\circ\text{--}105^\circ\text{C.}$  to constant weight. To convert the  $\text{AgCN}$  to silver, the Gooch crucible was transferred to an ordinary crucible of the same shape in which it just fitted, and ignited fairly strongly to constant weight. In the volumetric work (Series A) from 50–60 Gms. of the acid were weighed out similarly into a flask containing the  $\text{NaOH}$  or  $\text{NH}_3$ , respectively, and the whole diluted in a measuring flask to a definite volume, aliquot portions being drawn off for the titration.

The mean results by the gravimetric process may be taken as very close to the true strength by weight of HCN.

In Series A, below, the individual determinations were made on the same day as the gravimetric process, since the solution, even after mixing with the alkali, is not of constant strength.

The results may be regarded as fairly comparative. The amount of  $N/10$  silver solution varied from 40 to 46 Cc., so that the errors of reading are negligible in final results.

Measuring flasks, burettes, etc., were standard (verified at Charlottenburg).

The hydrocyanic acid used was prepared in the laboratory (from pure materials, by distilling  $\text{K}_4\text{FeCy}_6$  with dilute sulphuric) in order to ensure absence of  $\text{HCl}$  (a trace of which is said to be added to the commercial acid).

Presence of any free HCl would raise the apparent amount of HCN in the gravimetric and Volhard processes. The acid was diluted to contain rather less than 2 per cent. HCN.

All calculations and strengths of standard solutions were based on the International Atomic Weights, 1909; for silver, nitrogen and carbon the atomic weights are the same at the present day.

#### SERIES A.

Process.	(Results by weight in weight.)	
Gravimetric (as AgCN) (a) 1.650%; (b) 1.643%	} mean of 4 = 1.647%	
Gravimetric (as Silver) 1.648%; 1.645		(gravimetric).
Volhard (1 determination only) 1.651%		
Original Liebig (excess of NaOH slight)		mean of 6 = 1.650%
Fordos and Gelis		mean of 6 = 1.645%
Using NH <sub>3</sub> +KI		mean of 6 = 1.648%

#### SERIES B.

(Same stock of acid, but two months later.)  
Acid measured off by pipette (20 Cc.)

Original Liebig process.	Mean of 4 = 1.216 w/v.
Using borax	Mean of 4 = 1.215 w/v.
Using NH <sub>3</sub> +KI.	Mean of 4 = 1.213 w/v.

(All results obtained on the same day.)

The iodide method adopted was to use about equal volumes of 10 per cent. ammonia solution and dilute hydrocyanic acid, adding from 0.1 to 0.2 Gm. of KI. The results certainly seem to show that the end-point is sharper with this modification, especially when over 40 Cc. (as in Series B) of N/10 AgNO<sub>3</sub> was required. In this case using the same amount of HCN the amount of N/10 AgNO<sub>3</sub> required was 0.03 to 0.05 Cc. less than that required by Liebig's process.

#### ACTION OF GLYCERIN AS A PRESERVATIVE.

Williams (Y.B.P., 1874-1878) recommended the addition of glycerin for this purpose—20 per cent. was found to preserve the B. P. acid almost indefinitely. Some of the 1.65 per cent. acid of Series A was mixed with sufficient glycerin to make the mixture contain 25 per cent. glycerin. This was found to contain 1.23 per cent. HCN w/v. when made up. Nine months later it still contained 1.19 per cent.

The acid remaining after Series B analyses were finished was allowed to stand for the same period in diffused light. The strength was then 0.15%.

## SUMMARY.

It has been shown that Liebig's process for HCN properly conducted gives quite satisfactory results, but that Guerin's suggestion of using borax solution avoids the uncertainty that may occur through the use of too much alkali. Comparison of the B. P. process with that of the U. S. P. and the Codex shows that the B. P. apparently prescribes too little KI. However, if three or four times more KI is used the process agrees well with the gravimetric results. It seems probable that any defect in the B. P. process may be due to an insufficiency of iodide.

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YEAST ENZYMES.\*

All brewers are aware that considerable differences in attenuative power are exhibited by various brewery yeasts, but it is not so well known that this is in great measure due to the nature and quantity of the enzymes they secrete. According to our contemporary the (London) *Brewers' Gazette*, investigations by many scientific observers have proved the truth of this and one has to recognize the remarkable fact that ordinary brewers' yeast used very day is able to secrete a number of enzymes, and each of these have a specific function to perform in carrying out the complex reactions associated with fermentation. When the nature of these reactions is fully understood the relationship which exists between attenuative power and enzyme action becomes more apparent. The first enzyme to be discovered in yeast was invertase. This type of enzyme has the power of inverting cane sugar, and that present in ordinary worts is quickly converted into a mixture of dextrose and levulose before actual fermentation commences. So readily does this yeast enzyme act that a well-known process for making invert sugar in the brewery is based upon the action of this enzyme. The optimum temperature for effecting this process is about 130 degrees F.; but lower temperatures, such as those within the range of ordinary fermentation, are sufficient to enable this enzyme to exercise its action upon any cane sugar, generally present in small amount, which may find its way into the fermenting vessel. This inversion of cane sugar into equal proportions of dextrose and levulose must take place, before actual fermentation, caused by the enzyme zymase, can take place. It is nearly thirty years ago since J. O'Sullivan demonstrated that

\* From *Pure Products*, October, 1920.

this inversion takes place, under normal conditions, within the cell, since it was found that invertase cannot pass out of the yeast cell by exosmosis.

In a similar manner, maltose which is also a di-saccharide, like cane sugar, must also be reduced to a simpler form by the active agency of another enzyme before fermentation can take place. To this enzyme, the name maltase has been given, and while its presence was suggested by Bourguelot as long ago as 1866, its actual existence in yeast was only demonstrated by Emil Fischer and others in more recent years. Under normal circumstances, the decomposition of the di-saccharide maltose into the monosaccharide dextrose takes place within the yeast cell. As the result of these investigations it has been proved that neither a biose, triose or a polysaccharide is directly fermentable. All have to be reduced to the simpler monosaccharide or hexose form. At one time it was believed that certain moulds, *Monilia Candida*, for example, was able to ferment cane sugar without preliminary inversion, but later investigation showed that this organism contained an invertase which affected the hydrolysis of cane sugar in a similar manner to that of the yeast cell. In addition to the two sugars, cane sugar and maltose, brewers' wort also contains a number of complex carbohydrates, such as dextrin and intermediate bodies, known generally as malto-dextrins. These, as every brewer knows, have an important bearing upon the character and stability of beer, and have much to do with the condition and life which characterizes a well-brewed beer. It is quite obvious that some degradation of these substances takes place in cask, and fermentation proceeds, after the normal or primary fermentation has been completed, and this is due to the fact that certain yeast secrete diastase, and are, therefore, capable of hydrolyzing the complex carbohydrates slowly, and so enabling a gradual but steady fermentation to take place. Yeasts, and even the ordinary mixed yeasts of the brewery, differ in their capacity for cask fermentation, hence, in a perfect yeast, if one excludes the use of foreign yeasts, which do not readily accommodate themselves to a wort of beer, one requires the power of degrading certain complex carbohydrates, such as the so-called malto-dextrins. It is in this respect that the various types of yeast differ so much in respect to attenuative capacity. That *Saccharomyces Cerevisiae* is admirably suited to the fermentation of the brewers' worts is plain from a consideration of the enzymes enumerated. The cell contains

these entities for the degradation for nearly every carbohydrate found in ordinary worts. Its suitability for general purposes is more apparent when the characteristics of other saccharomyces are considered. For example, one well-known yeast, *Sacch. Apiculatus*, the pear-shaped cider yeast, possesses no hydrolyzing enzyme, and is, therefore, quite unable to ferment disaccharides, such as cane sugar, molasses, etc. Another yeast, *Sacch. Albicinus*, is able to hydrolyze and then ferment maltose, but contains no invertase, so that the cane sugar remains unchanged. On the other hand, *Sacch. Kephir*, the yeast employed in the fermentation of milk-yielding Koumiss, can ferment both sugar cane and lactose, but since it does not contain maltose, maltose is unaffected by its presence.

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#### AN HISTORICAL REVIEW OF THE PREPARATION OF QUININE SULPHATE IN JAVA AND IN BRITISH INDIA.\*

We are indebted to Herr P. Van Leersum, the former director of the Japanese Government cinchona plantation, whose decease we announced last week, for a valuable and interesting contribution on the development of the quinine industry in British India and in Java ("Algem. Landbouweekbl. v. Nederl. Ind.," No. 46, 1920). In his introductory remarks he states that the Indians are credited with having discovered the value of cinchona bark, whereas von Humboldt ascribes its introduction to Europeans, who casually discovered the bitter taste of the bark, and, in common with other bitter remedies, employed it in the treatment of fever. The Spanish doctor Villerobel was probably the first to bring some of the bark to Spain in 1632, and there it was first tested in 1639 by a priest in Alcada. Another tradition records that Don Jaun Lopez de Vega, medical attendant to Count Del Chinchon, Viceroy of Peru, received a quantity of cinchona bark from Don Jaun Lopez de Carnizares, Corrigedor of the province of Loja, and with it cured, in 1638, the wife of the Viceroy. On her return to Spain in 1640 she brought some of the bark with her, and thus laid the foundation of its use; in fact, for a long time it was known as *Pulvis comitissae*. The original home of the different varieties of cinchona is to be found in Boliva, Peru, Ecuador, Colombia, and Venezuela. The ruthless manner in which the bark was obtained led to the wholesale destruc-

\* From *The Chemist and Druggist*, August 28, 1920.

tion of the trees, and during the first half of the past century many travellers discussed the possibility of cultivating cinchona in other parts of the world. The first plantation of this valuable tree was undertaken by Markham in 1859 in British India, while the planting of seventy-five cinchona plants at Tjibodas in 1854 marked the beginning of its cultivation in Java. Prior to the isolation of its alkaloids, cinchona was used in the form of powdered bark, decoctions, extracts, etc. The following are the principal cinchona alkaloids:

Quinine, discovered by Pelletier and Caventou in 1820.

Quinidine, discovered by Henry and Delondre in 1833.

Cinchonine, discovered by Duncan in 1820, and made known by Pelletier and Caventou.

Cinchonidine, discovered by Winkler in 1848.

In addition there are numerous other substances present, such as quinamin, conchinamin, pariein, etc.

In view of the fact that about 95 per cent. of the bark is of no use to the manufacturer of quinine, it is evident that already at an early date in the history of quinine production steps were taken to obviate the necessity of conveying the whole bark a long distance to a factory—for instance, to Europe. Already in 1793 mention is made of an extract of cinchona prepared in South America, and in 1820 an extract of cinchona was imported into Hamburg bearing a label with "Extracto superior de Quina de la Fabrica de Benito Sebastian & Co., Cuzco." In 1841 there existed a quinine factory in Bolivia, but since the product was very impure it was little in request. Delondre, who was himself a manufacturer of quinine, erected in 1847 a factory in Valparaiso, which was closed in the following year. The first production of quinine in Asia took place at Ootacamund, in British India, and the author refers very fully to Broughton's enterprise in this connection. The method adopted by the latter fifty years ago is not without interest. Briefly, it consisted in boiling the fresh bark with 1 per cent. sulphuric acid; the liquid was then evaporated to one-sixth of its volume, transferred to a wooden vat and an excess of lime water added; after filtering, the precipitate was dried, mixed with alcohol, to which a little sulphuric acid was added, and by precipitation with caustic soda a product was obtained which Broughton called "amorphous quinine." This was stated to contain 18 per cent. of quinine, 54 per cent. of cinchonidine, 13 per cent. of cinchonine; amorphous

alkaloid and coloring matter together, 15 per cent. At that time the cost of production for one ounce amounted to one rupee, and it was sold by the Indian Government at the rate of 1 rupee 8 annas.

In 1873 C. H. Wood was intrusted by the British Government with the task of investigating the possibilities of preparing quinine from the Bengal plantations, particularly in Skikim. He followed practically the same method as adopted by de Vrij, which yielded an amorphous white powder, known in India as "Cinchona Febri-fuge" (in Java it was termed by de Vrij "Quinetum"), which in 1875 was sold by the Indian Government at 20 rupees a pound. The first attempts to manufacture alkaloids from the bark in Java were made in 1870, further investigations were undertaken in 1872 by Moens, and in 1877 Eydman introduced de Vrij's process. This consisted of extracting the bark with 1 per cent. hydrochloric acid for three days, and then precipitating the alkaloids by caustic soda. The residue was dissolved in dilute sulphuric acid and a precipitate obtained by the addition of caustic soda.

In 1900 Van Leersum secured the assistance of an expert staff at the Bandoeng factory, of which he was appointed director in 1902, and immediately set to work to solve the problem of the manufacture of pure quinine in Java. He then discussed the various factors which have to be considered in the manufacture of a pure product, and the difficulties that have to be overcome, which may be briefly referred to in the following points.

Calcium hydroxide is the best base for separating the alkaloids from the bark, but in order to render the cell walls permeable to the calcium hydroxide, the addition of sodium hydroxide is necessary, and powdered bark, calcium hydroxide, and sodium hydroxide must be intimately mixed. The relative proportions are 30 parts of fine slacked lime to 100 parts of finely powdered dry bark, and 90 parts of a 0.5 per cent. solution of sodium hydroxide for each 100 parts of bark. This mixture is placed in an extractor, and, under the circumstances, the best extractive is benzol with a high boiling point or toluol of 120 degrees C. boiling-point, which dissolves quinine 1:3. Petroleum and other earth oils have also been used as extractives; if the latter are employed the alkaloids are extracted by the addition of dilute sulphuric acid. If a substance is used which can be distilled off, *i. e.*, benzol, dilute acid is first added to retain the alkaloids in solution when removing the solvent by distillation. The acid solution of alkaloid is brought to boiling by steam, neutralized by the



addition of solution of caustic soda, and the solution of quinine is poured into crystallizing pans. The crude product is dissolved in dilute sulphuric acid, heated to boiling by steam, neutralized, and then filtered through charcoal. After crystallizing the crystals are centrifuged, washed and dried. The latter process has to take place in the dark, and red or yellow glass must be used for the windows of the room in which this is done, since quinine sulphate loses its white color on exposure to light. He mentioned that the appearance of the salt influences the price it commands—thus Howard's quinine is the highest quoted on the market owing to its fine appearance. The more voluminous it is the higher its value. Pure quinine sulphate does not yield such fine crystals as a product containing a certain amount of cinchonidine. Since the various pharmacopoeias permit the presence of a certain amount of cinchonidine in quinine, this is taken into consideration, and as Ledgeriana contains very little cinchonidine, Succirubra bark is mixed with the latter; Succirubra contains from 1 to 3 per cent. of cinchonidine.

The author then referred in detail to the manufacture of quinine from fresh bark by a process found after numerous experiments. Twenty-five grams of fresh bark are cut into small pieces and 2.5 grams of slaked lime are added. After pounding from five to ten minutes in a mortar the mass is sufficiently fine to be extracted. It is important to add exactly ten per cent. of slaked lime. It is best extracted with toluol of a boiling point of 120 degrees C., and then submitted to the process described above. Van Leersum, in conclusion, strongly advocated extensive trials to establish the advantages of manufacturing quinine from fresh bark, as this process would reduce the cost of production of this precious drug. He favored the creation of a government experimental laboratory, and referred to attempts made by quinine manufacturers to purchase the rights of this process, which is being found satisfactory, although worked on a modest scale with imperfect machinery, in the factory of K. A. R. Bosscha in Malabar. He reckons that the cost of producing one kilogram of quinine sulphate by this new process and making therefrom 5,000 tablets would amount to three florins, whereas the present cost of production amounts to 6.5 florins. It takes on an average 18 kilograms of dry bark to produce 1 kilogram of quinine sulphate, the average cost of 1 kilogram of bark being about 32 cents.

## AN IMPROVED METHOD FOR THE ASSAY OF ACONITE PREPARATIONS.\*

BY E. J. CHAPPEL, A.I.C., AND NOEL L. ALLPORT.

The standardization of tincture and liniment of aconite was made official for the first time in the 1914 edition of the British Pharmacopoeia. In the method to be adopted for their assay the analyst is left to base his process upon that described for the root. According to this method, the liquid preparation is evaporated to dryness at a temperature not exceeding 60°, and the solid residue is then dissolved in *N*/50 sulphuric acid. The resulting solution is next filtered but this operation is often so slow and tedious that a more expeditious method is needed. It is claimed that this disadvantage is overcome in the modified process here described.

It has been proposed by others to extract the acid liquid with ether, without previous filtration, but this gives troublesome emulsions, and we have found the use of petroleum ether to be much better, as there is no such tendency with this solvent. Other solvents were tried, but none was found to give such easy manipulation as petroleum ether. As the result of many experiments the following method is recommended:

15 Cc. of the liniment or 100 Cc. of the tincture are evaporated at a low temperature to remove the bulk of the alcohol. 5 Cc. of 10 per cent. sulphuric acid diluted with 20 Cc. of water are added, and the whole transferred to a separating funnel, with the assistance of a glass rod to break up the separated resin; the dish is then rinsed carefully with a little water.

About 20 Cc. of petroleum ether (B. P. 40°–60°) are added, and the mixture shaken. Separation is rapid, the aqueous liquor is drawn off and again shaken with petroleum ether. The two petroleum liquors are mixed, rinsed twice with water, and the washings added to the acid liquid, which is then rendered alkaline with ammonia and extracted four times with ether. The ethereal extracts are washed successively with the same portion of water, after which they are run into a flask and evaporated to dryness. The alkaloidal residue is dried at a low temperature to ensure removal of ammonia, and then titrated in the usual manner.

The great advantage is the saving of time in avoiding troublesome filtration, which may take several hours. The process may be

\*Reprinted from *The Pharmaceutical Journal and Pharmacist*, July 24, 1920.

equally applied to the assay of the root by first preparing a tincture as directed in the Pharmacopoeia.

The results obtained by this modified method are to all intents and purposes identical with those given by the more lengthy process of the British Pharmacopoeia, as the following table shows:

	ETHER SOLUBLE ALKALOIDS.	
	B.P. Process.	Modified Process.
Tincture	0.039 per cent.	0.035 per cent.
Liniment	0.199    "	0.206    "
"	0.193    "	0.196    "
"	0.193    "	0.196    "
"	0.209    "	0.212    "
"	0.257    "	0.254    "
"	0.196    "	0.193    "

These experiments have been carried out in the laboratories of The British Drug Houses, Ltd., to whom we are indebted for permission to publish the results.

## THE CAMPHOR INDUSTRY IN FOOCHOW.\*

BY VICE CONSUL ERNEST B. PRICE,  
 FOOCHOW, CHINA, JUNE 23, 1920.

Stocks of camphor now in the hands of local Foochow dealers are estimated at 80,000 pounds and of camphor oil at 40,000 pounds, while in the hands of the Government Camphor Bureau there are about 27,000 pounds.

The current market price in Foochow for camphor is 98 taels (\$98 at prevailing exchange rate) for 133 pounds, and for oil 40 taels (\$40) per 133 pounds. These prices are unusually low. About a year ago camphor was quoted at 200 to 220 taels. (At that time the tael was worth nearly \$1.50 United States currency, so that the price of camphor was between \$300 and \$330 per 133 pounds.) The causes of the present low prices seem to be three—governmental restrictions on production and distillation, lack of demand from Hong-kong, and a general slackening of business owing to difficulties of production and transportation.

There has been, however, a surprising amount of export, considering what conditions are. During the calendar year 1918, 56,533 pounds, valued at \$33,536, were exported from Foochow; in 1919,

\* *Commerce Reports*, Aug. 18, 1920.

931,600 pounds, valued at \$642,929, were exported; during the March quarter of 1920, 427,066 pounds, valued at \$268,413, were exported, representing a considerable increase.

*Methods of Distillation and Transportation.*—Trees fit to be used for camphor distillation must be at least 20 years old. When a suitable tree is found a crude native distillery is set up at the spot. This consists of a boiler, with an iron base and a wooden top, connected to a distilling vat partially filled with water. The camphor upon being conducted to the vat precipitates as crystals on the inner walls, while the nonprecipitable portions drop down as oil, which floats upon the water. About  $5\frac{1}{4}$  pounds of camphor and camphor oil, in the proportions of 70 per cent. camphor and 30 per cent. camphor oil, can be produced from 240 pounds of chips.

The districts where most of this initial distillation is done are Kienning, Yuchi, Yungan, Yenping, Tatien, Shaowu, Shawsien, and Ningte.

It is almost impossible to say how many men are engaged in the industry, but there cannot be many. Their wages are equal at the present rate of exchange to about \$0.38 a day.

The crude product is carried by porters to the Min River, or one of its tributaries, and then carried to Foochow by native boat. Boat hire is approximately \$1 per hundred pounds from the interior to Foochow.

*How Marketing Is Done.*—The marketing of camphor is done very largely through brokers in Hongkong. The distillers seldom do their own marketing, with the exception of the Japanese and Portuguese. There are also brokers in Foochow able to handle foreign orders in the English language.

It should be borne in mind that the camphor market is an extremely sensitive and dangerous one for the uninitiated. The factors of supply, governmental supervision, freights, stocks in Foochow and Hongkong, and three markets—Foochow, Hongkong, and the foreign market—all enter into the situation. Hence, no better scheme than the brokerage system can be suggested, unless the foreign buyer is prepared either to go into the producing end of it or into the buying and holding of considerable stocks himself.

The product as it leaves the distillery in the interior consists of crystals and camphor oil. The crystals are ready for marketing, but the oil is put through a process of redistillation at Foochow. This process is a simple one, and need not be described here in de-

tail. The effect is to distil from the oil all the remaining camphor; 133 pounds of oil produce 64 pounds of camphor and 27 pounds of desolated oil. The camphor derived from oil is of a cheaper grade than that derived originally from the wood chips. The desolated oil is used as a base for dyes and paints.

There are 12 of these distilleries in Foochow which produce camphor from the oil. They are known as the Yuan Cheng, Hsing Chi, Cheng Chi, Hsiang Chi, Fu Sheng, Hsieh Chi, Kao Fang, and Tao Ho—all Chinese; Ting Te—Portuguese; and Mitsui Bussan Kaisha and Tai Hua—Japanese. When working, each distillery produces on an average of 325 pounds of camphor a day.

*The Government Camphor Bureau.*—The various districts producing camphor have each an official camphor bureau under the control of the Provincial Commissioner of Industry. Each bureau has the authority to collect within the district it covers certain taxes and to buy camphor trees and distil camphor. In American currency the tax is approximately \$6 on every 133 pounds of camphor in transit. The taxes collected and the camphor produced are sent to another Government bureau called the Fukien Government Camphor Industry, Transportation, and Tax Collection Office. Its duties are to take in and turn over to the provincial government the taxes remitted by the various district bureaus and to take in and market the camphor received.

There is still a third bureau which has authority to buy camphor oil and distil it into camphor, marketing its product independently.

Private producers must take out licenses and agree to pay the taxes herein-before mentioned. There is also a license fee of \$2 local currency per month per vat.

Foreigners wishing to go or send into the interior to purchase camphor under what is known as the "transit pass" system, permitted by treaty, may still do so. Under this system the foreign exporter may bring the native product to the seaboard and export it to a foreign country by paying the regular 5 per cent. export duty plus a surtax of half the export duty. The foreigner may purchase either from the private producers or from the Government bureau. The effect of the Government bureau system is to tax the product just the same, because the foreigner may not operate his own distillery in the interior, and Government taxes are imposed on the distillery and its product before the foreigner purchases the camphor.

Japanese distillers operating in the city of Foochow are not

taxed, according to information given by the Japanese consulate in Foochow.

The Government bureau which markets the Government camphor announces that it sells at Hongkong market rates.

At present camphor is cheap and there are fairly large stocks on hand, but not much is coming in from the interior. Local firms are ready and anxious to do business with Americans.

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#### FURTHER REPORTS ON BENZYL BENZOATE.\*

Since benzyl benzoate was introduced into medicine little over a year ago, it has come into very general use in the treatment of diseases in which there is spasm of unstriated muscle.

T. E. McMurray (*N. Y. Med. Jour.*, July 24, 1920, p. 122) reports on its use in whooping cough, in which he obtained satisfactory and immediate results. The dose given was from 5 to 30 minims every four hours, depending on results. In some cases the smaller dose was sufficient, and in almost every case the paroxysms subsided. The effect was usually felt within 48 hours, and in one instance there was relief after the second dose. As a rule the relief is immediate and complete, and the treatment seems to lengthen the interval between attacks. No undesirable results were experienced; in one case a child of 12 months received 20 minims without showing any evidence of gastric or other disturbance.

D. I. Macht (*Johns Hopkins Hosp. Bull.*, July 1920, p. 236) found it acted as a valuable palliative, though not exactly curative, in a large number of cases of whooping cough that had resisted other treatment. He used a 20 per cent. alcoholic solution, giving from 5 to 40 drops in water three or four times a day or oftener, according to the age of the patient, and the severity of the disease. A few drops of benzaldehyde (essential oil of bitter almonds *sine* HCN) added to the solution not only makes the dose more palatable to children, but seems to increase the palliative effect.

D. I. Macht (*Med. Record*, July 24, 1920, p. 146) has found the drug most valuable in hiccough, not only in the mild form so common in infants, but in the more persistent forms which last for long periods of time. He cites several cases of persistent hiccough in adults in which relief was obtained with one or at most a few doses. Macht thinks that benzyl benzoate may also be of diagnostic value

\* From *The Prescriber*, October, 1920.

in differentiating between hiccoughs of purely central origin and those which are due to some peripheral cause. Inasmuch as the drug acts peripherally on the smooth muscle structures, he thinks that benzyl benzoate will prove most useful in hiccoughs of peripheral origin. He finds the drug acts best when administered in 20 per cent. alcoholic solution, in doses of from 20 to 40 drops in water or milk. Suspensions or emulsions are not satisfactory, and capsules have been found to cause local irritation, or to render the action too slow.

A. D. Hirschfelder (*Minnesota Med.*, Aug., 1920, p. 380) says that benzyl benzoate gives relief in many (though by no means all) cases of bronchial asthma. He has used it in other conditions of spasm, and has had striking results in the treatment of *dysmenorrhoea*.

E. A. Heller and E. Steinfield (*New York Med. Jour.*, July 31, 1920, p. 160) report on the *non-leucotoxic properties* of benzyl benzoate. Because of its close chemical derivation from benzol (benzene, B. P.), it appeared to them to be desirable to investigate any possible analogy to the toxic effects of the latter. Experiments were accordingly made on rabbits; several preliminary leucocyte counts were made in order to note any tendency to variation, and the animals were then given subcutaneous injections of a mixture of benzyl benzoate and olive oil, in equal parts. The dose varied from 1 Cc. to 2.5 Cc. per kilo of body-weight. Two animals were used as controls to demonstrate the destructive effects of benzol. Leucocyte counts were made daily until a tendency to consistency was noted and then every other day. The animals receiving benzyl benzoate showed no appreciable difference in leucocyte count, though those receiving the largest doses exhibited lethargy, weakness, and in one case death. In contrast, the two control animals receiving benzol showed definite evidences of depression of the leucocyte count, which later came back to approximately normal. The authors conclude that, unlike benzol, benzyl benzoate is without toxic effects upon the leucocytes and that there is a wide margin of safety between its therapeutic and its toxic doses.

D. I. Macht (*N. Y. Med Jour.*, Aug. 28, 1920, p. 269) reports on its use in some circulatory conditions. He finds the drug to possess powerful vasodilator properties, without being depressant to the heart when administered by the mouth in small doses. Owing to this property it has been found effective in the treatment of

hypertension and angina pectoris. The best method of administering the drug in such cases is in alcoholic solution which admits of rapid absorption and a control of the dose.

## THE EFFECTS OF AIR POLLUTION BY SMOKE AND ITS PREVENTION.\*

BY J. B. COHEN.

The Smoke-Abatement Committee, appointed by the Minister of Health, after taking a large amount of expert evidence, has issued an interim report on what may be termed "domestic smoke." The object of this report is mainly to furnish information as to the best methods of preventing smoke in connection with the new housing schemes to which the Ministry is offering large subsidies, and which consequently have to receive its approval. Incidentally, the destructive effects of coal smoke and the wastage of fuel, as well as the efficiency or otherwise of domestic heating appliances, have been considered. The annual loss of fuel in the form of soot is estimated at nearly two and a half million tons. At the same time, it is pointed out that the presence of soot is an indication that a far more formidable loss is being incurred by the inefficient utilization of the heat from the fuel. Moreover, domestic soot, by reason of its higher content of tar, which causes it to adhere to the objects upon which it falls, is far more destructive and dirt-producing than factory soot, which is a product of more complete combustion and contains less tar and more ash. The following analyses will make this clear:<sup>1</sup>

Constituents.	Original Coal.	Ordinary Grate Flue.	Top of Boiler Chimney —110 Feet.
Carbon.....	60.30	40.50	27.00
Hydrogen.....	4.89	4.37	1.68
Tar.....	1.64	25.91	1.14
Ash.....	8.48	18.16	61.80

As regards the effect of a smoky atmosphere on health, statistics show that a town fog immediately increases the death rate from respiratory diseases, and the cause underlying this high mortality,

\* From *Jour. Soc. Chem. Ind.*, Aug. 31, 1920.—Vide Interim Report of the Smoke-Abatement Committee of the Ministry of Health, 1920. H. M. Stationery Office.

<sup>1</sup> "Smoke, a Study of Town Air," by J. B. Cohen and A. G. Ruston. E. Arnold, London, 1912.



which invariably follows in the wake of a thick fog, must operate, though to a lesser degree, on the general health of the community in an industrial center under normal conditions. More definite evidence was forthcoming of the effects of smoke on vegetation. By shutting out sunlight, by covering the leaf and blocking the stomata with tar, life especially that of evergreen plants and trees is seriously affected. Moreover, the sulphuric acid which is invariably associated with soot, destroys the nitrifying organisms and removes lime from the soil as sulphate. This result has been observed at the experimental farm at Garforth attached to the University of Leeds, where the difference between limed and unlimed soils has exhibited in a remarkable way the action of acid soot. Another indirect result has been the diminished value of grazing land in smoke-infected areas, in consequence of which the rental of these pastures has steadily decreased from year to year.

Equally striking evidence was submitted to the Committee by Sir Frank Baines, Director of H. M. Office of Works, as to the serious damage occasioned to public and other buildings by smoke and other impurities in the atmosphere and especially by the deposit of acid soot. The effect in most cases was due to the removal of the calcium carbonate (which acts as a cement for grains of siliceous material) in the stone becoming dissolved as calcium sulphate and thus causing the siliceous particles to crumble away. In the opinion of Sir F. Baines, the cost of repairs and upkeep of public buildings and monuments (a very heavy expense) would be diminished by one-half if the smoke and the accompanying acid could be eliminated.

This acid soot not only clings to vegetation and to stone, but corrodes brick and metal work, attacks fabrics, leather binding of books, and discolors paint. The Manchester Air Pollution Advisory Board find, in Manchester, in the cost of washing materials alone apart from the labor involved, that more than £250,000 would be saved annually by the absence of smoke. A very careful and exhaustive inquiry by an expert committee of engineers, architects, and sciences estimated that in 1912, in Pittsburgh, U. S. A., the cost due to smoke was £4 per head of the population. If we take as a rough estimate the 20 towns of the United Kingdom of over 200,000 inhabitants having a total population of over 12 millions at 10s. a head, we get a sum of six millions, while the waste occurring accruing from the non-utilization of the by-products from raw coal, such as tar oils, sulphur, ammonia, and cyanogen compounds, so

essential to our chemical industries and motor traffic, must amount to many millions more.

A considerable amount of expert evidence was placed before this Committee on the efficiency of kitchen ranges, and on that of coke and coal burnt in an open fire by Prof. Barker of University College, London,<sup>1</sup> and Mrs. Fishenden,<sup>2</sup> of the Manchester College of Technology. There was a consensus of opinion that the old form of open kitchen range with back boiler was inefficient, wasteful in fuel and labor and productive of smoke.

For cooking, warming rooms, and providing a hot-water supply, the following recommendations were made by the Committee, and, in considering these they were guided by the utility, economy and efficiency of the proposals as regards smoke prevention. They do not recommend any one method, but make the following suggestions: That gas cookers and gas fires are thoroughly hygienic when properly installed; that where an adequate supply of gas is available, a gas-cooker should be substituted for the ordinary coal range; that for intermittent use both gas cookers and gas fires are often more economical than coal fires. That from a hygienic and labor-saving point of view electric cooking and heating have much to recommend them, but the present high price of electricity precludes their general adoption. The cheapest and most efficient method of producing a supply of hot water is a coke-fired boiler. A gas boiler, though more expensive, is very convenient in hot weather. The warming of rooms may be effected by hot-water radiators or gas fires, both of which are quite hygienic if the rooms are adequately ventilated. In this way coal may be dispensed with, and this system has been successfully established at the Austin Motor Company's village at Northfield, near Birmingham, where the warming of rooms by radiators and the hot-water supply were provided for by a coke stove and the cooking was done by gas. No coal entered the village and no smoke issued from it. The foliage and grass retained their fresh and clean appearance, and there was no discoloration of clothes and fabrics from the fall of soot. There is, however, a difficulty in dispensing with an open fire. Custom and sentiment are not easily eradicated, and there is no doubt that the appearance of warmth

<sup>1</sup> Vide Report of the Fuel Research Board for 1918-1919. Appendix B and p. 26.

<sup>2</sup> Coal Fires. By Dr. Fishenden, Air Pollution Advisory Board, Manchester City Council.

is even more important to the comfort of many people than its mere sensation. But this difficulty is in a fair way of being overcome. The production of what is known as low-temperature coke, or semi-coke, or "coalite," which ignites easily and glows with little or no smoke, is being investigated by the Fuel Research Board under the Department of Scientific and Industrial Research, and when this fuel is on the market at a moderate cost, and in sufficient quantity, the domestic smoke problem will be near solution. Meantime a coke stove which can be readily lighted is being perfected by a Halifax firm and has the advantage of being used as an open stove for warmth or closed for heating radiators or the boiler, or both, and for consuming kitchen refuse.

Hence efficiency, economy, cleanliness, and comfort can be obtained to-day if we choose without resorting to raw coal, thus producing an enormous national saving, with the added blessings of pure air, clear skies, and clean foliage.

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#### SIMPLE TESTS FOR ADULTERATION OF TURPENTINE.

Specialists of the Bureau of Chemistry, United States Department of Agriculture, have worked out simple tests for detecting the adulteration of turpentine, as follows:

Since the individual purchaser rarely has occasion and the producer is seldom in a position to make any extensive tests to determine whether a turpentine meets the specifications, it may be stated that the producer, knowing the purity of his product, need examine only to determine whether the turpentine is "standard" in color and whether it meets the specifications for specific gravity and distillation. Should the specific gravity at  $15.5^{\circ}/15.5^{\circ}$  C., when carefully taken with an accurate hydrometer or spindle, be between 0.862 and 0.870 ( $32.4^{\circ}$  to  $30.9^{\circ}$  Bé.), as is the case with nearly all American gum spirits of turpentine, it may safely be concluded that the sample will meet the requirements as to distillation. Should the specific gravity be found very close to the limits of the specifications adopted by the United States Government (0.862 to 0.875 at  $15.5^{\circ}$  C.), the sample should be examined by a competent chemist qualified to test turpentine. In the case of fresh turpentine which has not been scorched in making, become oxidized by standing in a tank, or been contaminated with oxidized turpentine, no testing is needed. Such turpentine will always pass the specified requirements.

When turpentine is adulterated to the extent of 10 per cent. or more, a careful observer familiar with turpentine can usually determine the fact by one or more of the following simple tests:

*Odor.*—The presence of kerosene, gasoline, benzol, or solvent naphtha is usually revealed by its odor. Wood turpentine is best distinguished from gum spirits by its odor. The odors of these materials cannot be described; they can be learned only by actual trial and experience. Lack of the characteristic turpentine odor is good ground for a careful test to determine the purity of the sample.

*Grease Spot.*—Pour a little of the suspected turpentine on a piece of white writing paper. If the bulk of the sample evaporates rapidly from the paper, leaving a greasy spot which evaporates very slowly or not at all, the turpentine is probably adulterated with kerosene or heavy solvent naphtha, or contains a large percentage of heavy turpentine which will not distil below  $170^{\circ}\text{C}$ . The odor of the grease spot often determines the nature of the adulterant. Greasy spots around bung or spigot holes of turpentine barrels are also indicative of these adulterants.

*Bead.*—When a perfectly clean dry bottle is partly filled with turpentine and violently shaken for a moment the head or foam that forms will immediately pass away if the turpentine is pure and fresh. If the foam persists for 5 seconds or more, the turpentine probably is adulterated or old.

*Evaporation Test.*—Set a 5-inch watch glass near an open window where a gentle air current can blow across it. Carefully place in it 5 cc. of the turpentine, so that the glass does not become wet with the turpentine beyond the edge of the surface of the liquid. Then carefully pipette or dip out 2 Cc., or about half of it. Observe the rim of the turpentine film after 3 hours. If the rim is continuous or more or less regular in outline, the turpentine is probably pure. If, however, the rim is made up of a chain of distinct drops or beads, or if the liquid appears to flow back to the center of the glass in distinct streams, it probably is adulterated with mineral oil or is an old turpentine of high specific gravity. The unevaporated residue will also smell of mineral oil if kerosene or any other oil which is less volatile than turpentine has been used as an adulterant.

Needless to state, if all these simple tests are definite, there can be little doubt that the turpentine is adulterated. When these tests are negative, however, it cannot be safely assumed that it is not adulterated to a small extent or very carefully to a large extent with a specially prepared turpentine adulterant or substitute.

## CURRENT LITERATURE.

### SCIENTIFIC AND TECHNICAL ABSTRACTS.

**TEST FOR FORMALDEHYDE IN MILK.**—Fuch sine furnishes a test for the presence of formaldehyde, the red color being turned to violet with a very small quantity. A. Gallego (*Revista Espanola de Med. y Cir.*, Jan. 1920, p. 10) recommends the employment of fuch sine as a test for the presence of formaldehyde in milk; the addition of a few drops of solution of fuch sine to a few Cc. of milk produces a pink tint, which deepens to violet when formaldehyde is present even in the dilution of 1:100,000. (From *The Prescriber*, October, 1920.)

**CANDELILLA WAX.**—Two Mexican *Euphorbiaceae*, *Pedilanthus pavonis* and *Pedilanthus aphyllus*, yield a wax known as candelilla wax, which is obtained by immersing the stems in boiling water and collecting the wax, which floats on the surface. The yield is about 3 per cent., and in view of the fact that this wax has recently been found in commerce and mistaken for a sophisticated sample of carnauba wax, Farcy (*Ann. fals. et fraudes*, p. 97, 1920) undertook an examination of candelilla wax, which yielded the following results:

Specific gravity.....	1.001 to 1.002
Melting point.....	64° to 65°
Free acids.....	18° to 19°
Total acids.....	66° to 67°
Iodine index.....	20° to 21°
Hydrocarbons.....	35 per cent.

(From *The Chemist and Druggist*, October 2, 1920.)

**PREPARATION OF EMETINE HYDROCHLORIDE.**—Dr. Juan L. Ague (*Boletín Farmaceutico*, Lima) asserts that the emetine hydrochloride of commerce is sometimes not a pure product, but contains a certain amount of cephaeline and psychotrine, to which the local irritant action on injection is attributable, and in addition has a less powerful amoebicide action than the pure alkaloid. He indicates the following method for preparing the pure salt: 200 Gms. of powdered ipecacuanha-root is exhausted with a mixture of 800 Cc. of ether and 400 Cc. of chloroform; after a few hours the mixture is shaken and 160 Cc. of 20 per cent. solution of ammonia added, and the whole allowed to stand for three hours. After adding 160 Cc. of distilled water and allowing to stand the liquid is decanted, treated with 4 per cent. hydrochloric acid, rendered alkaline by the addition of 20 per cent. solution of ammonia, whereupon it is ex-

tracted with 200 Cc. of ether to which a few Cc. of chloroform have been added. The ether is removed by distillation, and the residue—emetine—is treated with solution of caustic soda, which dissolves the cephaeline and psychotrine; the pure emetine is extracted by means of ether, and the hydrochloride is formed by the action of 4 per cent. hydrochloric acid on the pure alkaloid. (From *The Chemist and Druggist*, October 2, 1920.)

"CRESINEOL," A COMPOUND OF CINEOL AND *o*-CRESOL.—Cineol and oil of eucalyptus form a crystalline mass with *o*-cresol; no crystals are formed with *m*- or *p*-cresol. Molecular amounts of cineol at lab. temp. and *o*-cresol at 50 are mixed, when heat is developed, and, on cooling, white crystals appear, M. P. 55.2, B. P. 186.5–189. Soluble in ether, alcohol, chloroform, benzene, petroleum ether. Forms a colorless liquid with an equal weight of camphor. Does not appear to possess a caustic action on the skin. (S. Waldbott in *Chem. Abs.*, 14: 2967; T. T. Cocking, *Chem. and Drug.*, 93: 1032, 1920.)  
J. F. C.

XANTHORRHOEA RESINS.—Rennie, Cooke, and Findlayson report the following constituents found in an incomplete examination of three xanthorrhoea resins from Australia. All three contained *p*-coumaric acid, either free or as an ester, and *p*-hydroxybenzaldehyde. Steam distillation yielded the following substances not hitherto found in xanthorrhoea resins:

A.—A red resin from Kangaroo Island, species unknown, gave a small quantity of a liquid with an odor of vanillin; paeonol (2-hydroxy-4-methoxyacetophenone); and traces of a higher boiling substance.

B.—Yellow resin from X. Tateana (Kangaroo Island) gave a small quantity of unidentified fragrant liquid of vanillin odor; paeonol; hydroxypaeonol; and a small quantity of higher boiling constituent.

C.—Red resin from X. Preissii (W. Australia) gave a small quantity of unidentified fragrant liquid; 1-citronellol; paranol; paeonol; hydroxypaeonol; a compound, possibly oxydiphenyl ether; a small quantity of a high boiling constituent. (*J. Chem. Soc.*, 117: 338–50, 1920.)  
J. F. C.

DEMONSTRATION OF HEMIN CRYSTALS.—Strassmann describes a modification of the Teichmann test for the demonstration of hemin crystals in blood. Particles from the suspected blood stain are mixed

on a glass slide with a few drops of a mixture composed of one part of a five per cent. sodium chloride solution and either three or ten parts of concentrated glacial acetic acid, and covered with a cover-glass. The acid is evaporated in the usual manner over the flame. This mixture may be preserved, ready for use, for some time. (From *Münchener medizinische Wochenschrift*, Munich; through *Jour. Amer. Med. Assoc.*, October 2, 1920.)

ESTIMATION OF CAFFEINE IN COFFEE MIXTURES AND SO-CALLED CAFFEINELESS COFFEES.—E. Vautier (*Ann. Chim. anal. Appl.*, 1920, 2, 168-172.)—The method of estimating caffeine previously described (*Analyst*, 1918, 43, 410), gives sufficiently accurate results in the analysis of ordinary coffees, but in the case of coffees or mixtures poor in caffeine it is necessary to eliminate the sources of error in the sublimation process, either by estimating the nitrogen in the crude product or by purifying the residue of alkaloid. In the first method the crude caffeine is heated in a Kjeldahl flask with 10 Cc. of sulphuric acid, 5 Gms. of potassium sulphate, and 0.5 Gm. of crystallized copper sulphate, and the ammonia distilled, Congo red being used as indicator. A blank estimation should be made under the same conditions, each one Cc. of N/10 acid corresponds with 0.00485 Gms. of anhydrous or 0.00530 Gm. of hydrated caffeine. In the second method the solution of crude caffeine is evaporated to dryness on the water bath with 0.1 to 0.2 Gm. of sodium carbonate, and the residue repeatedly treated with small portions of chloroform, which does not dissolve the sodium salts of the humic acid-like impurities. The united filtrates from the insoluble residue are evaporated to dryness and the purified caffeine dried at 100° C. A caffeineless coffee yielded 0.13 per cent. of caffeine by the sublimation method, 0.05 per cent. calculated from the nitrogen, and 0.05 to 0.06 per cent. after purification with chloroform. (From *The Analyst*, September, 1920.)

IDENTIFICATION OF SULPHONAL AND TRIONAL.—W. Zimmermann (*Apoth. Zeit.*, 1920, 35, 27; through *Chem. Zeit. Rep.*, 1920, 44, 176.)—An odor of mercaptan is observed when 0.1 Gm. of sulphonal and trional is fused with 0.1 Gm. of sodium salicylate, and the mass then boiled with water; if 5 drops of alcohol and 5 drops of concentrated sulphuric acid are added, followed by a further 5 drops of the acid after one minute, and the mixture then warmed, a turbid red-colored solution is obtained having an odor of methyl salicylate.

A violet-colored residue is produced when 0.2 Gm. of either substance is ignited in a porcelain basin; the residue dissolves in a drop of water giving a violet-colored solution, the color changing rapidly to brown. The addition of a drop of hydrochloric acid produces a yellow color, the separation of a brown precipitate and liberation of sulphur dioxide. Santonin yields to a red coloration when heated with sodium salicylate. (From *The Analyst*, Sept., 1920.)

PARAGUAY TEA.—C. R. Hennings (*Ber. Deut. Pharm. Ges.*, 1920, 30, 22-26; through *Chem. Zeit. Rep.*, 1920, 44, 179.)—Analysis of Paraguay tea (maté) yielded the following results: Water, 9.00; water extract, 33.10; ash in water extract, 3.8; alkaloids, 2.1; tannin, 9.79; total ash, 6.62; soluble ash, 2.26; silica, etc., 1.44; alkalinity of ash (as  $K_2O$ ), 0.69; crude fiber, 15.45; ether extract, 9.8; volatile extract, 2.05; total nitrogen, 2.17; resins, 9.1 per cent. (From *The Analyst*, September, 1920.)

SILICA IN LEGUMINOUS SEED-COATS.—The author has found silica nodules in the palisade epidermis of the seeds of certain species of *Albizzia*, and also in that of *Afzelia cuanzensis* and *A. africana*, but not of *Vicia Faba*, or *Tamarindus indica*. The nodules measure up to three or four  $\mu$  in diameter, and occur just below the light-line. They are well shown in preparations treated with Schultze's maceration mixture and also by the phenol method, and may be found in the ash left by treating fragments of the seed-coats with concentrated sulphuric acid and incinerating. (*Archiv d. Pharm.*, 258, 138; through *The Pharm. Jour. and Pharmacist*, September 18, 1920.)

SUBSTITUTES FOR PLATINUM WIRE.—Borax beads may be made by heating the plumbago "lead" from a black lead pencil to redness, dipping it into powdered borax and then fusing the borax in the flame, so that the drop of melted borax is suspended at the end of the stick of graphite. The method of using a roll of pure filter paper instead of platinum wire, for flame tests, originally suggested by Eringhaus, is modified thus so as to give a longer lasting flame. The rolled slip is introduced into a small glass tube with a drawn out opening, and containing the liquid to be tested, or a solid substance moistened with hydrochloric acid. The end of the paper roll is allowed to project about 3 Cm. beyond the tube, to serve as a wick. This is then introduced into the flame, and the solution is fed to the wick by capillarity, just as in the case of an oil lamp or



candle. A long lasting flame test is thus obtained. (*J. Ind. Eng. Chem.*, 1920, 12, 500; through *The Pharm. Jour. & Pharmacist*, Sept. 4, 1920.)

UREA IN URINE.—M. Frenkel strongly recommends the xanthydrol method devised by Fosse (*Comptes Rendus*, 1913 and 1914) as being readily carried out and much more accurate than the hypobromite method, which is at best quite approximate. The reagent is a 1 in 10 solution of xanthydrol in methyl alcohol, and the urine should be adjusted to contain from 1 to 2 Gms. of urea in a liter. The determination is carried out as follows: Dilute 10 Cc. of the urine to 100 Cc.; add 35 Cc. of glacial acetic acid; then add at intervals of 10 minutes  $5 \times 1$  Cc. of the reagent, rotating each time; set aside for an hour, filter, wash with 20 Cc. of 95% alcohol in small portions, dry at 100°, and weigh. The weight divided by 7 gives the weight of urea. (*Ann. de Chemie Anal.*, ii, Vol. II, p. 234; through *The Pharm. Jour. & Pharmacist*, Sept. 4, 1920.)

ALBUMEN IN URINE.—M. G. Péguirier proposes the following modification of Méhu's method of determining albumin in urine by means of a solution of phenol and acetic acid in 90 per cent. alcohol: Triturate 10 Gms. of colorless phenol crystals with 10 Gms. of powdered citric acid and 20 Gms. of 95% alcohol in a mortar until dissolved, and filter; to a convenient quantity of the urine add acetic acid drop by drop until the reaction to litmus is distinctly acid, and filter off 50 Cc. Heat this in a beaker-flask until it just begins to boil, remove the source of heat, and add 5 Cc. of the phenol-citric acid reagent; rotate until the flocculent precipitate collects, filter through counterpoised double filter papers, wash with boiling water until the reaction is no longer acid, and then with ether-alcohol, dry at 100° and weigh, using the outer filter as counterbalance for the inner. The weight of the albumen multiplied by twenty gives the weight of albumen in a liter of urine. Urine that is highly albuminous must be appropriately diluted before acidification. The precipitation and washing are rapidly completed. (*Rep. de Pharmacie*, 76, p. 225; through *The Pharm. Jour. & Pharmacist*, Sept. 4, 1920.)

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#### NEWS ITEMS AND PERSONAL NOTES.

ADMIRAL STITT APPOINTED SURGEON-GENERAL OF THE NAVY.—President Wilson has appointed Rear-Admiral Edward Rhodes Stitt

Surgeon-General of the U. S. Navy to succeed Surgeon-General W. C. Braisted. Dr. Stitt graduated in Medicine from the University of Pennsylvania in 1889 and the same year entered the naval service as an assistant surgeon. He has been associated with the Jefferson Medical College of Philadelphia as a lecturer since 1907.

For some years his navy activities have been in the training of the medical officers entering the service and in directing the Navy laboratory and recently he has been in command of the Naval Medical School and he was one of the physicians called in consultation during President Wilson's serious illness. In 1917 he was promoted to the rank of Rear-Admiral.

Before entering upon the study of medicine, Dr. Stitt studied pharmacy and was graduated from the Philadelphia College of Pharmacy in 1887. He was accredited as a student from North Carolina. His thesis was upon the subject of Caffeine. At the annual commencement of that year he was awarded the John M. Maisch prize of \$20.00 in gold offered by Mr. J. H. Redsecker, of Lebanon, Pa., for histological knowledge of drugs.

Dr. Stitt was a delegate to the U. S. Pharmacopoeial Convention held in Washington in May last and was selected as a member of the Committee of Revision for the Tenth Revision now in preparation. The AMERICAN JOURNAL OF PHARMACY extends congratulations to Surgeon-General Stitt and looks forward to a record of accomplishments of the Department under his command. It is sincerely hoped that he will have as kindly interest in the welfare of the pharmacists in the Navy as was demonstrated by his predecessor.

H. K. MULFORD COMPANY IN NEW QUARTERS.—The H. K. Mulford Company have removed to their new home in the Mulford Building, 632-640 North Broad Street, Philadelphia. The executive offices and the pharmaceutical laboratories will be housed under one roof, the new building being nine stories in height and having nearly ten acres of floor space. Modern equipment and the best arrangement to facilitate the various steps in the manufacture of pharmaceuticals from the crude drugs to the finished products have been established.

NEW BUILDINGS OF THE MASSACHUSETTS COLLEGE OF PHARMACY. The new buildings of the Massachusetts College of Pharmacy on Linwood Avenue, Boston were thrown open to the inspection of pharmacists and their friends on Wednesday evening, December 1st.

The informal reception was largely attended. The AMERICAN JOURNAL OF PHARMACY is pleased to note the good fortune of this College, and extends its sincere best wishes for continued prosperity and progress.

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### BOOK REVIEWS.

A HISTORY OF CHEMISTRY FROM THE EARLIEST TIMES. By the late James Campbell Brown, D.Sc., LL.D., Professor of Chemistry in the University of Liverpool. Second edition, edited by Henry Hilton Brown. P. Blakiston's Son & Co., Philadelphia, 1920.

The literary executor of Prof. Campbell Brown has arranged in chronological sequence the series of lectures relating to the history and development of the science of chemistry that he was wont to give as part of his university course. An acquaintance with the history and the evolution of his calling is very rightly considered as an important part of the education of a professional student and the value of this book should appeal to every scholarly follower of this science.

This collection of historical data was first published in 1913 and the second edition now appearing attests its popularity and usefulness. Each of the fifty chapters is presumed to consider a distinct topic relating to some particular period, theory of the time, special problem of chemistry or philosophy accompanied by brief sketches of those then dominating the teaching of the chemical sciences or the events portrayed.

The author has divided the presentation of the lectures into two parts. Part I, Ancient History, considers the earliest developments of which we have knowledge and even that which, antedating our records, must be viewed as prehistoric down through the periods when the art of the magician and the fruitless search of the alchemists for the philosopher's stone that would "give perfection" and transmute the baser metals into gold held sway until about the beginning of the sixteenth century A.D. when the "alchemists altered their point of view—when they applied their minds to the search for knowledge instead of the search for gold.

In Part II, Modern Chemistry; in this is considered the progress of the chemical arts and the workers in that science since the dawn of the *Iatrochemical Period* about 1500 A.D. to the present date.

The closing chapter is devoted to The Radio Active Elements in which is briefly outlined the history and the work of the various contributors to the researches that have opened to human knowledge the far reaching facts and phenomena associated with this group of elements.

From the remotest time, the progress of the world has been very largely dependent upon chemical processes and the industrial development and the civilization of a period can be largely gauged by the scientific knowledge, especially chemical, possessed in the interval. The lecturer points out the ancient origin of the metallurgical processes, the making of glass, dyeing, and other industrial operations that are really chemical and also the very early acquaintance with antiseptics and their uses. From the most ancient type of alchemy, the Chaldean, the secrets and traditions were gradually transmitted from generations to generations and withal many grains of truth, disseminated amid the abundance of chaff of misconception and ignorance, have come down to be usefully applied in our day and generation. It is no small work to trace the progress of the ages, the vagaries of the philosophies, the principal actors of each period and their individual studies and contributions. Despite the fact that of many of these and their works but cursory glimpses are given the book is of great suggestive value as it lays the foundation for innumerable studies by students of the history of the science.

It is to be especially noted that until within a comparatively recent period, the leading chemists in most countries were physicians or pharmacists and this continued even after the entrance of the science into what the author terms the Iatrochemical Period. Many of their dissertations were based upon investigations carried on for the discovery of new remedial agents. The author declares that although Ambrose Godfrey wrote a "Compleat Course of Chemistry" in four folio volumes, he is best remembered as the originator of Godfrey's Cordial.

Many of those mentioned in this connection are names that are still associated with the studies and daily practices of pharmacy. For example, that distinguished investigator of his time John Rudolph Glauber, whose "*Sal Mirabile*" as Glauber's salt, is still a common and extensively used medicinal chemical. It was he who wrote, "it contenteth me that I have written the truth, and lighted a candle to my neighbour."

This posthumous work of Dr. Brown deserves to be read by every

student of chemistry and should for generations to come continue to serve the purpose of the author in preparing this course of lectures.

G. M. B.

NOTES ON CHEMICAL RESEARCH, AN ACCOUNT OF CERTAIN CONDITIONS WHICH APPLY TO ORIGINAL INVESTIGATIONS. By W. P. Dreaper, O.B.E., F.I.C. Small 8vo., xv, 195 pages. P. Blakiston's Son & Co., Philadelphia.

The author says in his preface that modern science is based on the record of past investigation, and the statement could have been appropriately supplemented by saying that as all who now practice a profession or make research have benefited by the labors of past workers, a sense of gratitude should lead every one to add a little to the store. The book in hand is of rather an exceptional type. Many books have been written to aid in specific lines of study and research, but this is rather a treatment of the philosophy of the subject with attention to the methods of training of those who are to undertake chemical investigations. To the mass of the statements, there will be no marked dissent. Every one who knows anything about science will agree that there is a need for active research, especially in English-speaking countries, in which the necessity of being independent of certain other countries has become painfully evident within the past decade. Mr. Dreaper quotes H. G. Wells, who makes a bitter denunciation of the "trained" investigator as contrasted with the "born" investigator, the latter being what we commonly call the "genius." It seems to the reviewer that Mr. Wells is hardly an authority in this field, and further, that the routine worker is of great service in science. The accumulation of data is a most important department of all scientific work. Dreaper, indeed, does not take Wells' view entirely to heart. There is a paragraph on references to journals, in which it is interesting to note that German sources are specifically mentioned, and further that nothing is said about American publications. The comprehensive and valuable literature that is now being issued on this side of the Atlantic is ignored. A chapter is devoted to The Student and His Course of Training, but it is limited to the specific training for research, nothing being said as to the earlier work. It would have been interesting to learn the author's view as to the comparative value of the classical and the so-called "practical" preliminary trainings, the latter being now much in vogue.

HENRY LEFFMANN.

TEXTBOOK OF PASTORAL AND AGRICULTURAL BOTANY. By John W. Harshberger, Ph.D., Professor of Botany, University of Pennsylvania. XIII. 294 pages and index, 121 illustrations. P. Blakiston's Son and Co., Philadelphia.

This interesting book, small in size though comprehensive in subjects considered, is from the pen of a teacher whose long experience in imparting botanical knowledge to students of general and professional courses has indicated what is most essential in economic botany, for readers to whom the text is particularly directed, namely, stock raisers, veterinarians and agriculturalists.

Its contents are grouped under eighteen chapters, as follows: 1. Stock-killing Plants. 2. Poisoning by Plants. 3. Poisonous Fungi and other Spore-bearing Plants. 4. Gymnospermous Poisonous Plants. 5. Monocotyledons as Poisonous Plants. 6. Dicotyledons as Poisonous Plants. 7. Loco Weeds and other Poisonous Plants. 8. Miscellaneous Dicotyledonous Plants. 9. Principally Solanaceous and Compositous Plants. 10. Feeds and Feeding. 11. The Structure and General Economic Importance of Grasses. 12. Description of Important Grass Forage Plants. 13. The Most Important American Cereals. 14. General Characteristics of the Leguminosae. 15. The Forage Plants of the Family Leguminosae. 16. Leguminous Root Tubercles and the Accumulation of Nitrogen. 17. Weeds and Weed Control. 18. Agricultural Seeds, Seed Selection and Testing.

Accompanying each chapter is a representative bibliography together with laboratory exercises and methods of utilizing the illustrative material mentioned.

In those portions of the text dealing with various poisonous plants a short description of the plant and its distribution is given. This is followed by the symptoms and treatment of the animals poisoned.

Many of the poisonous plants considered are those which are not usually found in textbooks of materia medica and toxicology, nor in the pharmaceutical journals which the average pharmacist receives.

Another useful feature of the book from the viewpoint of a pharmacist is the data contained in the chapter on Weeds and Weed Control. The pharmacist, being the one individual in the community mostly consulted on these matters, will find the information contained in this particular chapter quite profitable.

The extensive collection of useful subject matter and references found in this book should appeal alike to veterinarians, agriculturalists and economics botanists generally. The farmer, who should be aware of the kinds of weeds his stock is likely to feed upon, will find the text extremely useful and written in understandable language. For teachers and students in veterinary colleges this book satisfies a distinct need.

H. W. YOUNGKEN.

A TEXTBOOK OF ORGANIC CHEMISTRY. By E. DeBarry Barnett, B.Sc. (London), A.I.C. 360 pages. P. Blakiston's Son and Co., Philadelphia, 1920. Price, \$5.00.

The preface states that "this volume is intended as a companion volume to the author's 'Preparation of Organic Compounds.'" In it he "has endeavored to give a general survey of the most important classes of organic compounds. Emphasis has been laid on group reactions rather than on the reactions of individual compounds, so that the number of individual substances mentioned is smaller than is the case in most textbooks."

Chapter I discusses: the methods in general use for the elemental analysis, qualitatively and quantitatively, of organic compounds; the several methods for determining molecular weights; isomerism (including stereochemistry) and formulae; classification; nomenclature; and concludes with four pages on the literature of organic chemistry.

The remaining fifteen chapters are devoted to the Aliphatic Compounds (hydrocarbons, halogen derivatives, alcohols and mercaptans, ethers and sulphides, aldehydes and ketones, carboxylic acids, nitriles and analogous compounds, amines and similar compounds, amino acids and peptides, hydroxy, aldehydic and ketonic acids, carbohydrates) and the Aromatic Compounds (hydrocarbons, halogen compounds, nitroso and nitro compounds, amino compounds, sulphonic acids, alcohols, phenols and phenolic ethers, aldehydes, ketones, and quinones, diazo and diazo-amino compounds, azoxy, azo and hydrazo compounds, carboxylic acids and derivatives, anthraquinone and derivatives, triphenylamine dyes, alicyclic compounds, heterocyclic compounds, purines and alkaloids). For each class of compounds there is given: an explanation of the molecular structure, illustrated by formulas; the general methods for their preparation, illustrated by equations, or by formulas of compounds formed as steps in their synthesis; and statements re-

garding the general physical and chemical properties of the members of the class. The most important of the individual substances belonging to a class are described briefly, but in sufficient detail for most readers.

The author has succeeded in compressing a great deal of valuable information into a relatively small space, and at the same time has clothed it in language that is very readable and easily understood. At the end of nearly every chapter appears a bibliography of books treating particularly of the substances discussed in the chapter. The typography of the book leaves little to be desired. As is the case with most new books there are in it a few errors, none of them very serious and probably none that would escape detection by the careful reader.

The volume is such a one as can be used with profit by the beginner in the study of organic chemistry, as well as by the more advanced student who wishes to review the subject by touching chiefly its "high spots."

F. P. STROUP.

DR. FREDERICK C. WEBER'S SOLUTION OF THE CENTURY OLD PROBLEM: "IS THERE A CREATIVE POWER IN DISINTEGRATION IN THE UNIVERSE." A booklet of fifty-two pages, published by Farley & Frederick Publishing Company, Chicago, Ill., December, 1920. Price, \$1.00.

The author's statement of the question which he is endeavoring to solve is ambiguous. It might be taken to mean, Is there a Creative Power *in process of* Disintegration in the Universe? However, a study of the text shows that he really had in mind the question somewhat as follows: Is there a Creative Power *residing in, or evolved from,* the Disintegration *going on* in the Universe?

The opening paragraphs are given over to statements of axiomatic character, which the average reader readily concedes to be true. Matter, *per se*, is indestructible. Space is infinite. "Gravity is the first governing law of infinite space." "The second in importance of the governing laws, are a series of laws, which are the laws governing the combination of the elemental atoms into chemical molecules."

These latter laws the author formulates essentially as follows: "Every chemical molecule formed requires a definite amount of energy .... for its formation." "The energy required for the formation .... is as integral a component of the molecule .... as



are the atoms of the molecule." "When a chemical molecule is broken up, its component energy is liberated along with its atoms in exactly the same amount as that which was required for its formation." He claims originality in the formulation of "these three chemical laws." The statement is further made that elemental atoms can eternally combine, separate and recombine into new compounds under varying conditions. Also, the physical laws of force are stated to have "the same integral effect precisely in chemical combinations forming molecules as . . . in mechanics."

All of these are more or less well proven facts. The forms in which the author has expressed them, however, are very much involved. One can easily agree with Dr. Weber that "These basic natural laws, by their correlation, conclusively prove that there is a creative power," residing in, or evolved from the disintegration going on in the universe. It would seem that only a simple elucidation of this correlation would be required to give the answer to the problem under consideration.

A good part of the thesis is given over to an ingenious, but probably not original, discussion of the form of the atom. This is based upon the idea of geometric forms. The hypothesis is advanced that valency depends upon the number of plane surfaces possessed by the atom having any particular form. The atom of the hypothetical interspatial ether is considered as having a spherical form. The radium atom is pictured as a coiled spring, the uncoiled spring being the helium atom.

Just why the author cannot accept the usual theory that gravity is an attractive or pulling force, but must inject his idea of it, as a "pushing force," into the discussion is not clear. Apparently the usual conceptions regarding gravity would have served all the needs of his argument. He gives no satisfactory proof in support of his contention.

As one progresses in the study of the essay, what appears to be lack of mental clarity and of scientific exactness on the part of the author becomes more and more apparent. The following quotations will illustrate.

"Here on this axiomatic basis, rests the fact that every known science is an integral component of the *sun* of human knowledge, comprised within the entire range of the natural laws of the universe, so far as the human mind has discovered them. It is on this axiomatic basis that all natural laws act in perfect harmony, based on the

chemist's studies and knowledge of the ultimate atom or atoms and their chemical combinations as chemical molecules."

"Gravity being exerted throughout space, the bulging of the earth at the equator is what puts gravity's *equilibrium out of equilibrium* during its rotation in regular sequence and back again; and this is what forces the earth into an *eclipse* with its attendant changes in velocity in its orbit around the sun, and produces the tilting of the earth, and so produces the seasons." (The italics, of course, are the reviewers.)

The simple statement of an accepted scientific fact or law, without a direct, logical application of it to the problem in hand is not proof. Nevertheless, time after time, the author does this and claims the mere statement as proof of his contentions. In view of the lack of logical development of his proof, one is compelled to feel that the author cannot, with good conscience, <sup>T</sup>end his thesis with a *Quod erat demonstrandum*.

G. M. B., JR.

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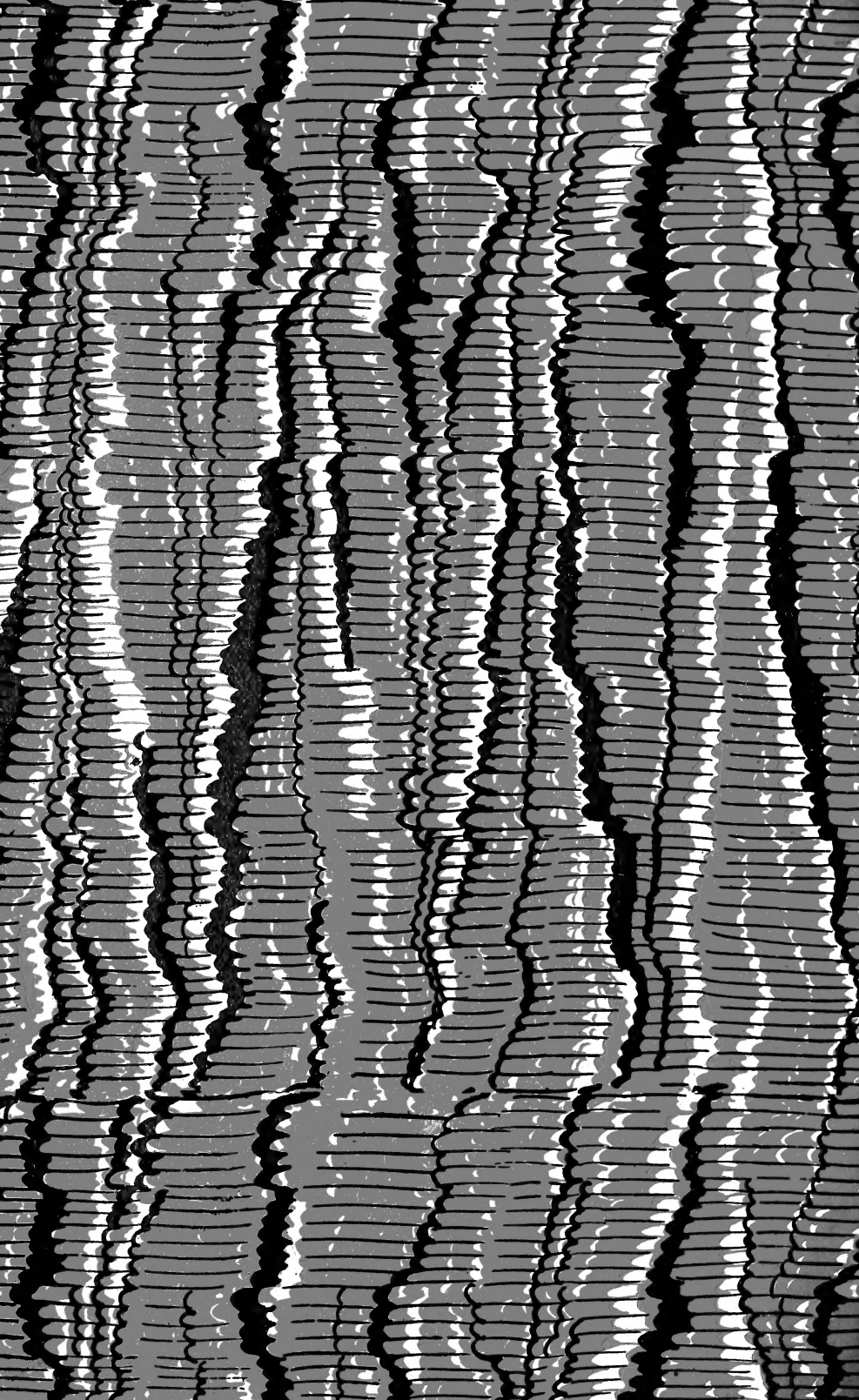


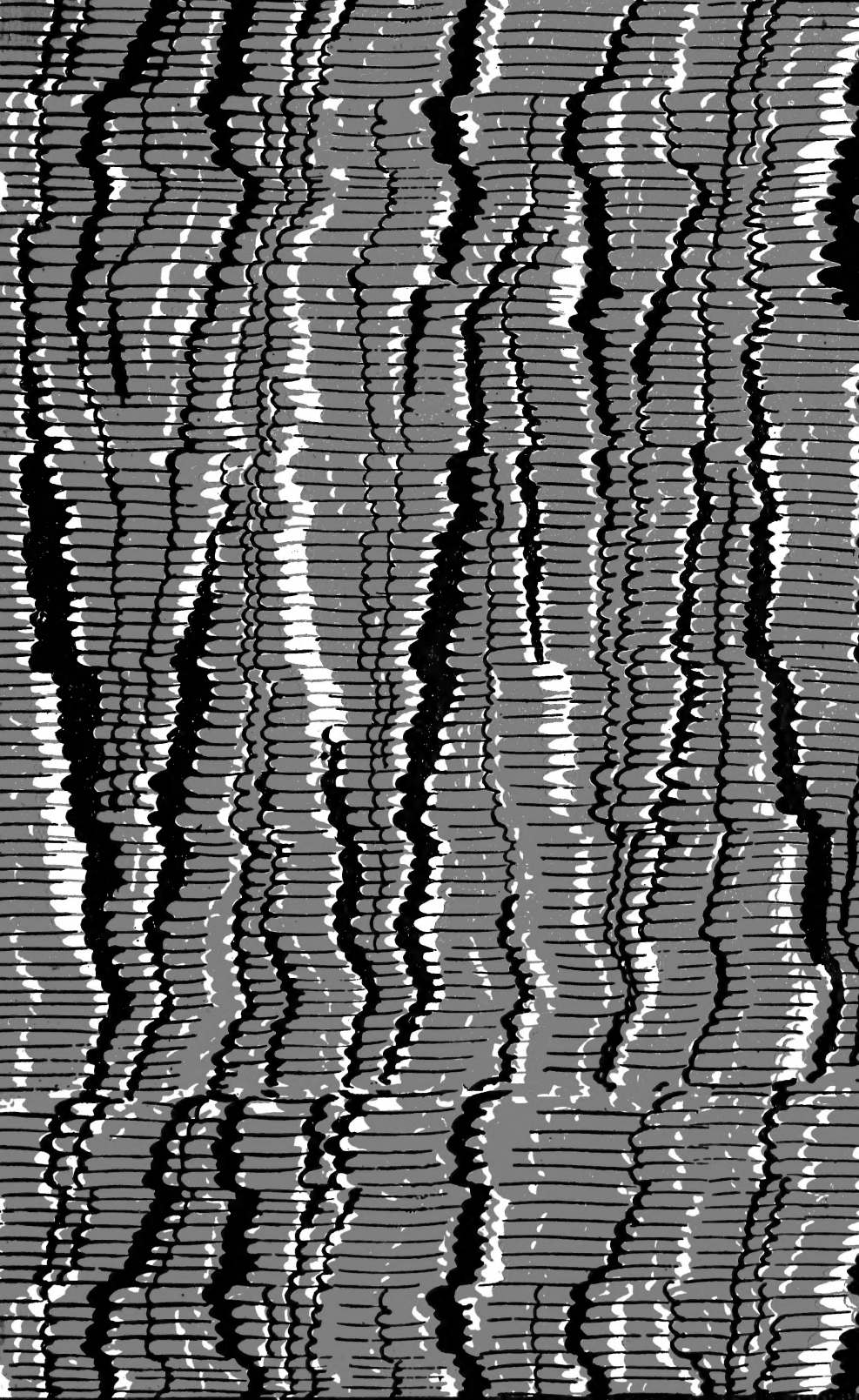












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